

## ORIGINAL RESEARCH

# Occupational pesticide use and self-reported olfactory impairment in US farmers

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**ABSTRACT**

**Objectives** Pesticide exposure may impair human olfaction, but empirical evidence is limited. We examined associations between occupational use of 50 specific pesticides and olfactory impairment, both self-reported, among 20 409 participants in the Agricultural Health Study, a prospective cohort of pesticide applicators (mostly farmers, 97% male).

**Methods** We used logistic regression models to estimate odds ratios (OR) and 95% confidence intervals (CI) for associations between pesticide use at enrolment (1993–1997) and olfactory impairment reported two decades later (2013–2016), adjusting for baseline covariates.

**Results** About 10% of participants reported olfactory impairment. The overall cumulative days of any pesticide use at enrolment were associated with a higher odds of reporting olfactory impairment (OR (highest vs lowest quartile): 1.17 (95% CI: 1.02 to 1.34), p-trend = 0.003). In the analyses of 50 specific pesticides, ever-use of 20 pesticides showed modest associations with olfactory impairment, with ORs ranging from 1.11 to 1.33. Of these, higher lifetime days of use of 12 pesticides were associated with higher odds of olfactory impairment compared with never use (p-trend ≤ 0.05), including two organochlorine insecticides (dichlorodiphenyltrichloroethane and lindane), two organophosphate insecticides (diazinon and malathion), permethrin, the fungicide captan and six herbicides (glyphosate, petroleum distillates, 2,4-dichlorophenoxyacetic acid, 2,4,5-trichlorophenoxyacetic acid and metribuzin), although many of these did not exhibit clear, monotonic exposure-response patterns.

**Conclusion** Overall, we found relatively broad associations between pesticides and olfactory impairment, involving many individual pesticides and covering several chemical classes, suggesting that pesticides could affect olfaction through multiple pathways. Future epidemiological studies with objective measurement of olfaction are required to confirm these findings.

**Key messages****What is already known about this subject?**

- Pesticide exposure may impair olfaction, but empirical evidence is very limited.
- We know of only one epidemiologic investigation linking specific pesticides with olfactory impairment.
- That study, conducted within the Agricultural Health Study (AHS), found that unusually high pesticide exposure events are associated with higher odds of reporting a poor sense of smell, but it did not focus on long-term use of pesticides.
- Olfactory impairment increases with age, is common in patients with neurodegenerative diseases, and could be an early sign of future neurodegenerative disease.

**What are the new findings?**

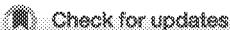
- We report the first evidence of associations between chronic occupational exposure to many individual pesticides (covering several chemical classes) and olfactory impairment reported many years after exposure.

**How might this impact on policy or clinical practice in the foreseeable future?**

- Because they represent the earliest evidence for associations between occupational uses of specific pesticides and self-reported olfactory impairment, these findings warrant confirmation in studies with objectively assessed sense of smell.

and overall quality of life<sup>3</sup> and has been associated with increased mortality in older adults.<sup>4,5</sup> Olfactory impairment is likely an early manifestation of neurodegenerative conditions including Parkinson's and Alzheimer's diseases<sup>6,7</sup> and thus may be critical to understanding the process of early neurodegeneration. Although research on modifiable risk factors for olfactory impairment among older adults could have major public health significance, empirical data are limited.

Exposure to pesticides can occur through occupational or residential use, or indirectly from air drifts, food, and water or soil contamination. Although poorly studied, pesticide exposures may jeopardise human sense of smell through several



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**INTRODUCTION**

Olfactory impairment is common among older adults, affecting about 25% of those 50 years or older and over 60% of those older than 80 years.<sup>1,2</sup> Olfactory deficit may negatively impact human functioning such as safety, diet and nutrition,

mechanisms.<sup>8</sup> Direct contact with inhaled pesticides may damage peripheral olfactory epithelium through acute or chronic inflammation. Further, inhaled or ingested pesticides may exert neurotoxic effects on the central nervous system including central olfactory pathways through several mechanisms, leading to olfactory deficit.<sup>8–10</sup> Prior evidence linking certain pesticides or their functional classes (eg, organochlorine insecticides dichlorodiphenyltrichloroethane (DDT) and dieldrin, organophosphate insecticides and herbicide paraquat) with neurocognitive dysfunction and Parkinson's and Alzheimer's diseases provides indirect support for the pesticide-olfactory impairment hypothesis.<sup>11–14</sup> Several toxicological studies have also shown olfactory impairment in animals exposed to certain pesticides (including organophosphate insecticide malathion and herbicide paraquat).<sup>15–17</sup> An investigation in the Agricultural Health Study (AHS) reported the first evidence that unusually high pesticide exposure events are associated with higher odds of reporting a poor sense of smell.<sup>18</sup> Here, we evaluated possible associations between chronic occupational exposures to specific pesticides and self-reported olfactory impairment in the same population.

## METHODS

### Study population

In 1993–1997, 52 394 private pesticide applicators (97.4% male, mainly farmers) enrolled in the AHS by completing an enrolment questionnaire at local pesticide licensing locations.<sup>19</sup> Participants were also asked to complete an additional take-home questionnaire, which was returned by 44% ( $n=22\,916$ ) of the enrollees. Those who returned the take-home questionnaire were largely similar,<sup>20</sup> but more likely to be older, from Iowa, and former or never smokers than those who did not (online supplemental table 1). Participants were also asked to report pesticide application practices, other farm exposures, sociodemographics, lifestyle and medical history. Follow-up interviews were conducted in 1999–2003, 2005–2010 and 2013–2016 to update information on farm exposures and medical history. Participants were asked about olfactory impairment at the third follow-up in 2013–2016, which was completed by 24 145 applicators. All study questionnaires can be found at <https://aghealth.nih.gov/collaboration/questionnaires.html>. All applicable institutional review boards approved the study.

### Self-reported pesticide use

#### Pesticide exposure at enrolment

The enrolment questionnaire asked about general pesticide use including days and years participants personally mixed or applied pesticides. The questionnaire also sought information on ever-use of 50 specific pesticides and duration and frequency of use for 22 of them. The take-home questionnaire further asked participants to provide duration and frequency of use for the remaining 28 pesticides. These questionnaires also asked for detailed information on pesticide use practices including application methods, mixing processes, personal protective equipment use, and other workplace hygiene factors.

Our primary analyses focused on pesticides reported at enrolment, and we used two exposure metrics: ever-use and exposure intensity-weighted lifetime days of use (IWLD) as measures of cumulative exposure to pesticides. The IWLD was estimated as the product of years of use and days used per year weighted by exposure intensity and then grouped into four categories: never use (referent category) and tertiles of days use among users. Exposure intensity weight was derived using an algorithm that incorporated information on mixing practices, application

methods, repair of pesticide application equipment and personal protective equipment use. Details on its development are described elsewhere.<sup>21</sup>

#### Pesticide exposure at the first follow-up

We also considered cumulative pesticide use (ie, IWLD) through the first follow-up in our secondary analyses. At the first follow-up, applicators were asked to provide the names and number of days of use for each pesticide that they used in the year before the interview or, for pesticides that they no longer used, in the most recent year of use. Participants also provided information on pesticide application practices. To estimate cumulative exposure through the first follow-up, we assumed that pesticide usage reported in the most recent year represented pesticide use during the period since enrolment.

### Self-reported olfactory impairment

In the third follow-up (2013–2016), participants were asked 'do you suffer from a loss of sense of smell or significantly decreased sense of smell?' Positive response to the question was considered 'olfactory impairment'. Participants were also asked 'when did you start losing your sense of smell?' with four response choices: ≤1, 1–5, 5–10 and >10 years prior to the third follow-up.

### Statistical analysis

Of the 24 145 who completed the third follow-up questionnaire, we excluded 2549 participants with proxy-provided responses, 402 missing information on olfaction and 785 with missing data on baseline covariates that were selected for confounding adjustment. For ever-use analyses and for the IWLD analyses for the 22 pesticides for which frequency and duration of use were asked in the enrolment questionnaire, our overall analytical sample included 20 409 applicators. In the IWLD analyses for the 28 pesticides for which frequency and duration of use were asked only in the take-home questionnaire, our overall analytic sample size was 11 847. Sample sizes for individual pesticide analyses differed due to missing data on specific pesticides.

We used logistic regression models to estimate odds ratios (OR) and 95% confidence intervals (CI) for the association between pesticide use at enrolment and olfactory impairment reported about 19 years later (on average, range: 16–22 years) in the third follow-up, adjusting for baseline age (continuous linear function), sex, state of residence, education, smoking status and other farming tasks (including repairing engines, replacing asbestos brake linings, handling stored grain, working in swine confinement areas, welding, and painting). These common farming activities may result in exposures to airborne irritants (eg, dusts, fumes, solvents, and metals), which may in turn damage olfaction.<sup>8</sup> For age at enrolment, we further explored other functional forms including quadratic terms, restricted quadratic splines and age categories and got similar results. We therefore adjusted age as a continuous linear variable throughout the analyses. We also adjusted for ever-use of specific pesticides that were correlated with the pesticide of interest (with Spearman correlation coefficient  $\geq 0.40$ ). In the IWLD analyses, we estimated p for trend using the median value for each exposure category as a continuous variable in regression models. For all the analyses, exposures were modelled as a fixed variable (not time varying) in relation to the outcome.

To examine the robustness of our results, we conducted six sensitivity analyses. First, we conducted analyses using two other exposure metrics—lifetime days of use (not weighted by exposure intensity) and average days per year of use. Second, we

performed analysis excluding individuals who reported a history of head injury or were missing data on head injury among those who returned the take-home questionnaire ( $n=10\,162$ ) (head injury was reported only on the take-home questionnaire). Third, we excluded participants who self-reported Parkinson's disease in any AHS surveys because olfactory impairment is one of the most common prodromal symptoms of Parkinson's disease ( $n=20\,184$ ).<sup>6,22</sup> Fourth, we restricted to participants who reported olfactory impairment with onset reported  $\leq 10$  years before the third follow-up to reduce the possibility of reverse causality ( $n=19\,563$ ). Fifth, we examined associations between IWLD of pesticides through the first follow-up and olfactory impairment with onset reported  $\leq 10$  years before the third follow-up to account for more proximal exposures ( $n=19\,563$ ); for this analysis as well, IWLD was modelled as a fixed variable (not time varying). Because some participants did not participate in the first follow-up survey, in this analysis, we used multiple imputation to estimate cumulative exposure for those who did not complete the first follow-up (16%). Details on imputation are described elsewhere.<sup>23</sup> Lastly, as only about 40% of the enrollees completed the third follow-up survey, we applied inverse probability of censoring weights to see if selective attrition of the cohort over time biased our results.<sup>24</sup> We performed statistical analyses using SAS V9.4 (SAS Institute). Statistical significance was determined using two-sided tests with  $\alpha$  of 0.05.

## RESULTS

The average age at enrolment was 46 years (SD: 11 years; range: 15–87); 97% were male and 98% white. About 10% reported olfactory impairment ( $n=2069$ ) about two decades later at the third follow-up. Of these, 1223 reported the loss  $\leq 10$  years before the third follow-up, 617 reported loss  $> 10$  years before and 229 did not respond to the question on time of onset. Older participants, those from Iowa, current smokers, and those involved in activities including repairing engines, replacing asbestos brake linings, and welding more likely to report olfactory impairment (table 1). Further, participants with head injury at baseline and those who reported having Parkinson's disease in any AHS survey were more likely to report olfactory impairment.

In the analysis of lifetime days of use of any pesticides, compared with the lowest usage quartile, the OR for the highest quartile was 1.17 (95% CI: 1.02 to 1.34,  $p$  for trend=0.003, table 2). In the ever-use analyses, 20 of the 50 specific pesticides examined were significantly associated with olfactory impairment, including four organochlorines (dieldrin, DDT, toxaphene, and lindane), two carbamates (carbaryl and carbofuran), four organophosphates (chlorpyrifos, dichlorvos, malathion, and parathion), permethrin (both on animal and on crop use), the fumigant carbon tetrachloride/carbon disulfide 80/20 mix, two fungicides (captan and metalaxyl), and six herbicides (dicamba, glyphosate, paraquat, petroleum distillates, 2,4-dichlorophenoxyacetic acid (2,4-D), and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T)); ORs were mostly modest, ranging from 1.11 to 1.33 (table 2). Although not statistically significant, several other pesticides had ORs of similar or higher magnitude (eg, coumaphos and chlothralonil; table 2). The results were generally similar when we excluded those with head injury among those who returned take-home questionnaire (online supplemental table 2) or excluded self-reported Parkinson's disease (online supplemental table 3). When we restricted analyses to participants who reported olfactory impairment with onset  $\leq 10$  years before the third follow-up, results were generally similar, although associations for a few pesticides were no longer significant (eg, toxaphene

**Table 1** Characteristics of participants at enrolment in the Agricultural Health Study ( $n=20\,409$ ), Iowa and North Carolina

Characteristics	No OI, n (%) (n=18\,340)	OI, n (%) (n=2069)
Age (years)*		
$\leq 45$	9220 (50.3)	812 (39.2)
>45–55	5098 (27.8)	584 (28.2)
>55–65	3332 (18.2)	520 (25.1)
>65	690 (3.8)	153 (7.4)
Sex		
Female	528 (2.9)	48 (2.3)
Male	17\,812 (97.1)	2021 (97.7)
Race†		
Other	291 (1.6)	25 (1.2)
White	18\,033 (98.4)	2042 (98.8)
State*		
Iowa	12\,765 (69.6)	1500 (72.5)
North Carolina	5575 (30.4)	569 (27.5)
Marital status*‡		
Never married	1636 (8.9)	129 (6.2)
Married/living as married	15\,911 (86.9)	1845 (89.3)
Divorced/widowed	773 (4.2)	93 (4.5)
Education		
$\leq$ High school	9591 (52.3)	1057 (51.1)
1–3 year beyond high school	4820 (26.3)	584 (28.2)
$\geq$ College graduate	3929 (21.4)	428 (20.7)
Smoking status*		
Never	10\,496 (57.2)	1037 (50.1)
Former	5666 (30.9)	726 (35.1)
Current	2178 (11.9)	306 (14.8)
Chewing tobacco use		
No	15\,825 (86.3)	1790 (86.5)
Yes	2515 (13.7)	279 (13.5)
Snuff use		
No	17\,534 (95.6)	1977 (95.6)
Yes	806 (4.4)	92 (4.4)
Alcohol intake (past 12 months)‡		
No	5720 (32.1)	619 (30.9)
Yes	12\,081 (67.9)	1386 (69.1)
Ever diagnosed with head injury* ¶***		
No	9114 (87.3)	1048 (83.6)
Yes	1325 (12.7)	205 (16.4)
Repair engines*		
No	10\,264 (56)	1103 (53.3)
Yes	8076 (44)	966 (46.7)
Replace asbestos brake linings*		
No	15\,402 (84)	1676 (81)
Yes	2938 (16)	393 (19)
Handle stored grain		
No	4823 (26.3)	524 (25.3)
Yes	13\,517 (73.7)	1545 (74.7)
Work in swine confinement areas		
No	12\,736 (69.4)	1431 (69.2)
Yes	5604 (30.6)	638 (30.8)
Weld		
No	5144 (28)	539 (26.1)
Yes	13\,196 (72)	1530 (73.9)
Paint		
No	5144 (28)	569 (27.5)

continued

Table 1 continued

Characteristics	No OI, n (%) (n=18 340)	OI, n (%) (n=2069)
Yes	13196 (72)	1500 (72.5)
Parkinson's disease *†‡‡	18237 (99.6)	1947 (94.8)
No	70 (0.4)	106 (5.2)

\* p value from  $\chi^2$  tests  $\leq 0.05$ .

†Race missing: n=18.

‡Marital status missing n=22.

§Alcohol intake missing: n=603.

¶Head injury missing: n=8717.

\*\*Information on these variables was asked only in the take-home survey (completed by 44% of the enrollees).

††Parkinson's disease missing n=49.

‡‡All characteristics except for Parkinson's disease were asked at enrolment; self-reported Parkinson's disease at enrolment or at any follow-up to the third.

OI, olfactory impairment.

and lindane); results for other pesticides became stronger (eg, DDT and fumigant carbon tetrachloride/carbon disulfide 80/20 mix) (table 2).

In the IWLD analyses (table 3), we found statistically significant trends ( $p$  for trend  $\leq 0.05$ ) for two organochlorine insecticides (DDT and lindane), two organophosphate insecticides (diazinon and malathion), permethrin use on crops, the fungicide captan, and six herbicides (glyphosate, metolachlor, petroleum distillates, 2,4-D, 2,4,5-T, and metribuzin). Although ORs were generally elevated for higher exposure categories compared with never use, for some of these, OR estimates did not show a clear, monotonic exposure-response pattern. For metolachlor, the trend was inverse. Results were generally similar when we excluded self-reported Parkinson's disease cases from the analysis (online supplemental table 4).

The results were similar when we used unweighted lifetime days of pesticide use (online supplemental table 5). However, in the analysis that examined average days per year of use, we noted that associations were much stronger for those who reported more frequent days per year and that dose-response was more apparent than for other lifetime measures for organochlorine insecticides toxaphene (OR for the highest day category: 2.31 (95% CI: 1.26 to 4.25)) and lindane (OR: 3.07 (95% CI: 1.76 to 5.35)), fungicide metalaxyl (OR: 1.74 (95% CI: 1.11 to 2.73)) and herbicides paraquat (OR: 2.06 (95% CI: 1.13 to 3.75)) (online supplemental table 6).

When we restricted analyses to participants who reported olfactory impairment with onset reported  $\leq 10$  years before the third follow-up (table 3), overall results were similar but the  $p$  for trend for a few pesticides were no longer statistically significant; these results were similar to those examining IWLD of pesticides through the first follow-up in relation to olfactory impairment with onset reported  $\leq 10$  years before the third follow-up (online supplemental table 7). In the analysis that examined ever-use of pesticides in relation to olfactory impairment using inverse probability of censoring weights, the results were generally similar (online supplemental table 8).

## DISCUSSION

In this large epidemiologic study of US farmers, we found that occupational use of pesticides was associated with higher odds of reporting olfactory impairment. The association seems to be relatively broad, not limited to just a few pesticides and involving several chemical classes. The results were consistent across

several sensitivity analyses. Overall, our data offer novel empirical evidence supporting the notion that occupational exposures to pesticides may harm human sense of smell.

Few epidemiological studies have explored the association between pesticides and poor olfaction in humans. There have been case reports of anosmia in individuals reporting exposure to unusually high levels of pesticides.<sup>25 26</sup> Other studies have examined farming in relation to olfaction, but findings are inconsistent.<sup>27–29</sup> For example, a study of olfaction among pesticide-exposed Latino farmworkers compared with non-farm workers (primarily construction or production workers) from North Carolina found no difference in performance in odour identification between the two groups, but found that farmworkers performed poorly compared with non-farmers in an olfactory threshold test.<sup>29</sup> This difference in olfactory threshold between the groups persisted over a 2-year follow-up period.<sup>28</sup> In contrast, another study conducted among attendants of an agricultural trade show in Nebraska found no association between farming and olfactory function.<sup>27</sup>

In a prior analysis of AHS farmers, a history of unusually high pesticide exposure events was associated with elevated olfactory impairment, and the association was stronger if there was a longer delay in cleaning with soap and water.<sup>18</sup> These associations were statistically significant for the organochlorine insecticides DDT and lindane and the herbicides alachlor, metolachlor, 2,4-D, and pendimethalin. Notably, our current investigation also found similar associations for occupational use of organochlorine insecticides DDT and lindane for both ever-use and IWLD analyses and for the herbicide 2,4-D among the highest users compared with never users. To our knowledge, no epidemiologic studies have found specific pesticides to be associated with olfactory impairment. However, Bello and Dumancas<sup>30</sup> reported an association for urinary levels of 2,4-dichlorophenol (a precursor and environmental degradate of 2,4-D and other chlorophenols) and olfactory impairment among participants aged  $\geq 40$  years in a cross-sectional analysis of the 2013–2014 National Health and Nutrition Examination Survey data.

Our study is the first epidemiological study to comprehensively examine occupational use of pesticides and olfactory impairment among farmers. We found modest associations with several pesticides. These observations are biologically plausible as pesticides may cause olfactory impairment via both peripheral and central nervous systems.<sup>8 10</sup> Inhaled pesticides may damage the olfactory epithelium and olfactory receptor neurons by inducing oxidative stress, acute or chronic inflammation, and pathophysiological changes (eg, hyperplasia and metaplasia). Pesticides that find their way to the brain via olfactory structures, by bypassing the blood brain barrier, or via ingestion may affect olfaction-associated central nervous system processes and neurotransmitter systems resulting in diminished olfactory abilities. Further, pesticides that enter through the olfactory structures or the digestive tract may initiate synucleinopathy in the olfactory bulb and the gut, which may later spread to brain, as posited by the Braak hypothesis.<sup>9</sup> Over time, these peripheral and central mechanisms may individually or synergistically contribute to age-related olfactory impairment and neurodegeneration.

Pesticides have also been shown to alter olfactory function in animals including honeybees, fish, and rodents.<sup>15–17</sup> For example, intraperitoneal administration of paraquat in rats has been shown to impair olfactory discrimination ability.<sup>15</sup> Similarly, exposures to the organophosphate insecticides diazinon<sup>31</sup> and malathion<sup>32</sup> and herbicide glyphosate<sup>16</sup> have been shown to alter olfactory responses in salmonids. The pesticides diazinon, malathion, and glyphosate, either ever-use or IWLD,

**Table 2** General pesticide use and ever-use of pesticide at enrolment in relation to self-reported olfactory impairment reported in the third follow-up in the Agricultural Health Study (n=20409), Iowa and North Carolina

Pesticides	Any OI* (n=20409)		Time-restricted OI† (n=19563)		
	No OI n (%) (n=18340)	OI n (%) (n=2069)	OR (95% CI)‡	OI n (%) (n=1223)	OR (95% CI)‡
Overall pesticide lifetime days					
0 to 64	4867 (26.5)	499 (24.1)	Ref	302 (24.7)	Ref
>64 to 225	6042 (32.9)	607 (29.4)	0.93 (0.82 to 1.06)	353 (28.9)	0.92 (0.79 to 1.09)
>225 to 458	3959 (21.6)	461 (22.3)	1.04 (0.91 to 1.19)	253 (20.7)	0.96 (0.80 to 1.14)
>458	3469 (18.9)	501 (24.2)	1.17 (1.02 to 1.34)	314 (25.7)	1.18 (1.00 to 1.40)
Insecticide	17260 (94.1)	1989 (96.2)	1.37 (1.08 to 1.74)	1172 (95.9)	1.31 (0.97 to 1.76)
Organochlorine	9720 (54.5)	1330 (65.7)	1.26 (1.13 to 1.41)	788 (66.2)	1.20 (1.05 to 1.38)
Aldrin	3251 (19.4)	517 (27.6)	1.04 (0.90 to 1.20)	314 (28.6)	1.06 (0.88 to 1.27)
Chlordane	4492 (26.4)	657 (34.1)	1.10 (0.98 to 1.24)	398 (35.0)	1.07 (0.93 to 1.24)
Dieldrin	1161 (6.9)	217 (11.5)	1.19 (1.00 to 1.43)	123 (11.2)	1.06 (0.85 to 1.34)
DDT	3951 (23.4)	666 (34.8)	1.27 (1.11 to 1.44)	425 (37.7)	1.33 (1.13 to 1.56)
Heptachlor	2817 (16.8)	454 (24.1)	1.09 (0.94 to 1.26)	278 (25.2)	1.16 (0.96 to 1.40)
Toxaphene	2412 (14.2)	367 (19.2)	1.20 (1.06 to 1.37)	213 (18.9)	1.12 (0.95 to 1.32)
Lindane	3663 (21.5)	521 (26.9)	1.19 (1.06 to 1.33)	289 (25.3)	1.10 (0.95 to 1.27)
Carbamate	12244 (68.0)	1537 (75.4)	1.38 (1.23 to 1.54)	923 (76.7)	1.41 (1.22 to 1.63)
Aldicarb	1694 (10.1)	171 (9.0)	0.93 (0.77 to 1.12)	115 (10.3)	1.05 (0.83 to 1.32)
Carbaryl	9611 (56.5)	1204 (62.5)	1.21 (1.09 to 1.36)	717 (63.6)	1.21 (1.05 to 1.40)
Carbofuran	4976 (29.1)	672 (34.5)	1.16 (1.04 to 1.28)	397 (34.5)	1.13 (1.00 to 1.29)
Organophosphate	16507 (90.0)	1934 (93.6)	1.45 (1.20 to 1.75)	1135 (93.0)	1.37 (1.08 to 1.73)
Chlorpyrifos	7884 (43.3)	963 (46.8)	1.15 (1.04 to 1.26)	568 (46.7)	1.15 (1.02 to 1.30)
Coumaphos	1634 (9.7)	222 (11.6)	1.15 (0.99 to 1.34)	125 (11.0)	1.09 (0.89 to 1.32)
Diazinon	5648 (33.2)	720 (37.4)	1.07 (0.96 to 1.19)	428 (37.9)	1.05 (0.92 to 1.21)
Dichlorvos	2123 (12.4)	309 (15.9)	1.22 (1.07 to 1.40)	175 (15.2)	1.20 (1.01 to 1.42)
Fonofos	4057 (23.6)	497 (25.4)	0.99 (0.89 to 1.11)	286 (24.7)	0.99 (0.86 to 1.15)
Malathion	12742 (72.8)	1579 (79.1)	1.29 (1.15 to 1.45)	928 (78.7)	1.26 (1.09 to 1.47)
Parathion	2554 (15.1)	363 (18.9)	1.21 (1.07 to 1.38)	221 (19.6)	1.19 (1.01 to 1.40)
Phorate	6001 (35.2)	741 (38.4)	1.01 (0.91 to 1.12)	433 (38.1)	1.01 (0.89 to 1.16)
Terbufos	7105 (41.2)	864 (44.0)	1.07 (0.97 to 1.18)	503 (43.5)	1.09 (0.96 to 1.23)
Trichlorfon	104 (0.6)	16 (0.8)	1.31 (0.77 to 2.24)	8 (0.7)	1.03 (0.50 to 2.13)
Permethrin (crops)	2327 (13.7)	303 (15.7)	1.23 (1.07 to 1.40)	177 (15.5)	1.23 (1.04 to 1.45)
Permethrin (animals)	2638 (15.3)	342 (17.5)	1.21 (1.06 to 1.38)	202 (17.5)	1.30 (1.10 to 1.53)
Fumigant	4197 (22.9)	531 (25.7)	1.15 (1.02 to 1.29)	336 (27.5)	1.18 (1.03 to 1.37)
CCl <sub>4</sub> /CS <sub>2</sub>	955 (5.6)	171 (8.9)	1.28 (1.07 to 1.53)	111 (9.8)	1.40 (1.13 to 1.73)
Aluminium phosphide	913 (5.4)	112 (5.8)	1.06 (0.86 to 1.30)	71 (6.3)	1.16 (0.90 to 1.49)
Ethylene dibromide	619 (3.6)	66 (3.4)	0.86 (0.66 to 1.12)	43 (3.8)	0.91 (0.66 to 1.26)
Methyl bromide	2395 (14.0)	258 (13.4)	0.98 (0.82 to 1.17)	162 (14.3)	0.94 (0.75 to 1.17)
Fungicide	6529 (35.6)	767 (37.1)	1.14 (1.03 to 1.27)	469 (38.4)	1.15 (1.00 to 1.31)
Benomyl	1513 (9.1)	176 (9.4)	1.00 (0.80 to 1.24)	107 (9.7)	0.93 (0.71 to 1.22)
Captan	2087 (12.3)	288 (14.9)	1.21 (1.06 to 1.39)	170 (14.8)	1.22 (1.03 to 1.45)
Chlorothalonil	1153 (6.8)	142 (7.4)	1.23 (0.99 to 1.52)	91 (8.0)	1.27 (0.98 to 1.66)
Maneb	1523 (8.9)	187 (9.7)	1.12 (0.91 to 1.37)	117 (10.3)	1.12 (0.87 to 1.43)
Metalaxyl	3749 (21.9)	434 (22.5)	1.15 (1.00 to 1.31)	268 (23.7)	1.16 (0.98 to 1.38)
Ziram	253 (1.5)	28 (1.5)	0.98 (0.66 to 1.46)	20 (1.8)	1.18 (0.74 to 1.87)
Herbicide	17913 (97.7)	2035 (98.4)	1.23 (0.85 to 1.78)	1199 (98.1)	1.09 (0.70 to 1.68)
Alachlor	9641 (55.8)	1161 (59.4)	1.06 (0.96 to 1.17)	680 (58.7)	1.04 (0.92 to 1.18)
Butylate	5776 (34.1)	720 (37.6)	1.03 (0.92 to 1.15)	416 (36.9)	1.00 (0.87 to 1.16)
Chlorimuron ethyl	6482 (37.9)	734 (38.1)	1.00 (0.91 to 1.11)	436 (38.4)	1.04 (0.92 to 1.18)
Dicamba	9506 (55.2)	1158 (59.3)	1.11 (1.00 to 1.24)	658 (57.1)	1.08 (0.94 to 1.25)
EPTC	3658 (21.5)	448 (23.1)	1.04 (0.93 to 1.17)	257 (22.4)	1.04 (0.89 to 1.21)
Glyphosate	14086 (77.2)	1678 (81.5)	1.33 (1.18 to 1.50)	991 (81.4)	1.31 (1.13 to 1.53)
Imazethapyr	7892 (46.9)	903 (47.4)	0.94 (0.84 to 1.05)	511 (45.5)	0.93 (0.81 to 1.08)
Metolachlor	8338 (48.3)	978 (49.7)	1.02 (0.93 to 1.13)	577 (49.6)	1.06 (0.93 to 1.20)
Paraquat	3905 (22.8)	480 (24.9)	1.15 (1.02 to 1.29)	294 (25.8)	1.13 (0.97 to 1.32)

continued

Table 2 continued

Pesticides	Any OI* (n=20409)		Time-restricted OI† (n=19563)		
	No OI n (%) (n=18340)	OI n (%) (n=2069)	OR (95% CI)‡	OI n (%) (n=1223)	OR (95% CI)‡
Pendimethalin	7663 (44.6)	885 (45.7)	1.04 (0.94 to 1.14)	534 (46.8)	1.09 (0.96 to 1.23)
Petroleum distillates	8490 (49.9)	1070 (55.5)	1.16 (1.05 to 1.28)	631 (55.6)	1.19 (1.05 to 1.35)
Trifluralin	9091 (55.5)	1111 (60.0)	1.07 (0.95 to 1.21)	637 (58.4)	1.03 (0.89 to 1.19)
2,4-D	14175 (78.0)	1692 (82.3)	1.14 (1.00 to 1.29)	992 (81.5)	1.11 (0.95 to 1.31)
2,4,5-T	3738 (22.1)	563 (29.4)	1.22 (1.08 to 1.39)	343 (30.5)	1.24 (1.06 to 1.45)
2,4,5-TP	1666 (9.9)	221 (11.5)	0.88 (0.74 to 1.04)	138 (12.3)	0.91 (0.73 to 1.12)
Atrazine	13400 (73.4)	1579 (76.9)	1.09 (0.97 to 1.22)	929 (76.5)	1.10 (0.94 to 1.27)
Cyanazine	7748 (44.9)	949 (48.5)	1.06 (0.95 to 1.17)	562 (48.6)	1.13 (0.98 to 1.29)
Metrubuzin	8089 (49.0)	1012 (54.1)	1.08 (0.96 to 1.21)	590 (53.6)	1.13 (0.97 to 1.31)

\*All olfactory impairment cases.

†Olfactory impairment with onset reported ≤10 years before the third follow-up.

‡ORs are adjusted for age, sex, state of residence, education, smoking status, ever performed following tasks at least once each year (repair engines, replace asbestos brake linings, handle stored grain, work in swine confinement areas, weld and paint) and correlated pesticides (correlated ever-use of pesticides with Spearman correlation ≥0.40); correlated pesticides are not adjusted for overall lifetime days.

CCl<sub>4</sub>/CS<sub>x</sub>, carbon tetrachloride/carbon disulfide 80/20 mix; 2,4-D, 2,4-dichlorophenoxyacetic acid; DDT, dichlorodiphenyltrichloroethane; EPTC, S-ethyl dipropylthiocarbamate; OI, olfactory impairment; 2,4,5-T, 2,4,5-trichlorophenoxyacetic acid; 2,4,5-TP, 2-(2,4,5-trichlorophenoxy) propionic acid.

were also linked with olfactory deficits in our current analysis. Some of these pesticides associated with olfactory impairment were also associated with Parkinson's and Alzheimer's diseases and poor cognitive function in prior studies.<sup>11 12 14</sup> For example, the organophosphate insecticides diazinon, malathion and parathion,<sup>33</sup> the fungicide captan,<sup>34</sup> the herbicides paraquat,<sup>12</sup> 2,4-D,<sup>35</sup> and 2,4,5-T<sup>36</sup> have been associated with Parkinson's disease. Likewise, higher serum levels of DDT were associated with increased risk for Alzheimer's disease.<sup>14</sup> While our study limits us from making causal inferences about pesticides' roles in the development of olfactory impairment and their relevance to prodromal neurodegeneration, current findings may provide clues for future investigations.

The 10% prevalence of self-reported olfactory impairment in the current study is similar to the prevalence observed in other studies.<sup>1 2 37</sup> However, self-reported olfactory impairment is subject to error. Self-reported olfactory impairment has low sensitivity (ranging from <20% to >60%) but good specificity (ranging 80% to >90%) compared with objective smell identification tests that are often the choice for use in epidemiologic studies.<sup>1 2 37</sup> Self-reported olfactory impairment relies on one's ability to notice potential impairment and cannot differentiate various modalities of the impairment (eg, identification vs threshold or discrimination). Further, we asked about olfactory impairment once about 20 years after study enrolment, and we used predefined categories to capture age at onset. Future epidemiological studies need to confirm our findings with objectively evaluated olfactory impairment and to assess whether pesticide exposures impact various domains of olfaction.

We considered a range of covariates and co-exposures as potential confounders in our analysis; still, some of the observed associations could be explained by inadequate control of confounding. For example, the AHS did not collect information on conditions such as chronic sinonasal disease that may affect both olfaction and pesticide use, and information on head injury and a history of high pesticide exposure events was available only for the subset that returned the take-home questionnaire. Additionally, we did not consider

other environmental exposures in our analysis that may have confounded our results.

Information on specific pesticides was also based on self-reports. However, self-reports can capture lifetime exposures better than biomarkers that only represent a snapshot of pesticide use given the short half-lives of most pesticides. AHS pesticide applicators have been shown to provide reliable and plausible information on specific pesticide uses. For example, in a subsample of 4088 AHS participants in Iowa who completed the same questionnaire 1 year after their enrolment, the agreement for ever/never use of specific pesticides and application practices ranged from 70% to >90%, although somewhat lower agreement, ranging from 50% to 71%, was found for duration, frequency and decade first applied for the specific pesticides.<sup>38</sup> Further, in a comparison of AHS participant's responses on the decade of first use and duration of use for specific pesticides to the year the pesticides were first registered for use in the USA, <7% reported first use before pesticide registration date and <5% participants overestimated their duration of use.<sup>39</sup>

We restricted our analysis to those who completed the third follow-up when we first asked about olfactory deficit. Selective attrition that may have resulted from pesticide exposure or factors associated with olfactory dysfunction may have biased our results. We did not observe any influence on effect estimates when we corrected for potential selection bias using inverse probability of censoring weights, and a prior AHS study also suggested no evidence of bias when exposure and outcome are not strongly associated with participation (as likely in our current investigation).<sup>40</sup> However, we cannot rule out potential selection bias. In addition, we made multiple comparisons and some findings could be due to chance.

Further, our results may not be generalisable to populations with relatively lower levels of pesticide exposure or to seasonal or other farmworkers who are more racially and socioeconomically diverse than our study participants. Lastly, the current study focused on pesticides that were commonly used at the time of enrolment or in the past and did not account for pesticide exposure changes since the first follow-up. Future studies on pesticides and olfaction should focus on newer pesticides as well

**Table 3** Intensity-weighted lifetime days of use of pesticides at enrolment in relation to self-reported olfactory impairment reported in the third follow-up in the Agricultural Health Study (n=20 409), Iowa and North Carolina

Pesticides	Exposure*	Any OI† (n=20 409)			Time-restricted OI‡ (n=19 563)			
		No OI (n (%))	OI (n (%))	OR (95% CI)	P trend	OI (n (%))	OR (95% CI)	
<b>Insecticide</b>								
Organochlorine								
Aldrin§	Never	8080 (83.9)	849 (75.7)	Ref	0.25	477 (74.2)	Ref	0.3
	>0–315	565 (5.9)	96 (8.6)	1.10 (0.86 to 1.41)		59 (9.2)	1.16 (0.85 to 1.58)	
	>315–952	489 (5.1)	77 (6.9)	1.00 (0.76 to 1.31)		47 (7.3)	1.05 (0.74 to 1.48)	
	>952	501 (5.2)	99 (8.8)	1.18 (0.91 to 1.53)		60 (9.3)	1.21 (0.88 to 1.68)	
Chlordane§	Never	8080 (82.0)	857 (73.2)	Ref	0.08	500 (74.2)	Ref	0.35
	>0–231	580 (5.9)	108 (9.2)	1.46 (1.17 to 1.83)		58 (8.6)	1.29 (0.96 to 1.73)	
	>231–637	607 (6.2)	104 (8.9)	1.29 (1.03 to 1.63)		55 (8.2)	1.12 (0.83 to 1.52)	
	>637	586 (5.9)	102 (8.7)	1.24 (0.98 to 1.56)		61 (9.1)	1.16 (0.87 to 1.56)	
Dieldrin§	Never	9363 (96.7)	1074 (94.5)	Ref	0.63	615 (94.9)	Ref	0.17
	>0–210	114 (1.2)	22 (1.9)	1.06 (0.66 to 1.70)		14 (2.2)	1.12 (0.63 to 2.00)	
	>210–653	94 (1.0)	23 (2.0)	1.31 (0.82 to 2.11)		12 (1.9)	1.15 (0.61 to 2.14)	
	>653	111 (1.1)	17 (1.5)	0.82 (0.49 to 1.40)		7 (1.1)	0.55 (0.25 to 1.21)	
DDT§	Never	7873 (81.3)	794 (69.5)	Ref	0.02	440 (66.7)	Ref	0.01
	>0–328	601 (6.2)	115 (10.1)	1.33 (1.06 to 1.68)		71 (10.8)	1.40 (1.05 to 1.86)	
	>328–1583	622 (6.4)	113 (9.9)	1.26 (1.00 to 1.59)		67 (10.2)	1.23 (0.91 to 1.65)	
	>1583	592 (6.1)	121 (10.6)	1.38 (1.10 to 1.74)		82 (12.4)	1.54 (1.17 to 2.03)	
Heptachlor§	Never	8535 (88.1)	938 (82.4)	Ref	0.32	545 (83.6)	Ref	0.88
	>0–289	396 (4.1)	60 (5.3)	0.99 (0.73 to 1.33)		37 (5.7)	0.99 (0.68 to 1.43)	
	>289–893	384 (4.0)	71 (6.2)	1.18 (0.89 to 1.56)		30 (4.6)	0.81 (0.54 to 1.20)	
	>893	374 (3.9)	69 (6.1)	1.13 (0.85 to 1.51)		40 (6.1)	1.05 (0.73 to 1.50)	
Toxaphene§	Never	9303 (90.1)	1050 (85.7)	Ref	0.27	613 (86.5)	Ref	0.66
	>0–298	344 (3.3)	57 (4.7)	1.26 (0.94 to 1.69)		33 (4.7)	1.25 (0.86 to 1.81)	
	>298–1050	335 (3.2)	67 (5.5)	1.49 (1.13 to 1.96)		33 (4.7)	1.24 (0.85 to 1.80)	
	>1050	344 (3.3)	51 (4.2)	1.12 (0.82 to 1.53)		30 (4.2)	1.06 (0.72 to 1.57)	
Lindane§	Never	8777 (85.5)	957 (78.4)	Ref	<0.0001	552 (78.3)	Ref	0.0006
	>0–315	513 (5.0)	83 (6.8)	1.31 (1.03 to 1.68)		45 (6.4)	1.27 (0.92 to 1.75)	
	>315–1176	498 (4.9)	85 (7.0)	1.42 (1.11 to 1.82)		54 (7.7)	1.62 (1.20 to 2.18)	
	>1176	474 (4.6)	95 (7.8)	1.64 (1.29 to 2.07)		54 (7.7)	1.60 (1.18 to 2.17)	
<b>Carbamate</b>								
Aldicarb§	Never	9177 (93.3)	1099 (94.3)	Ref	0.09	629 (93.6)	Ref	0.33
	>0–613	213 (2.2)	25 (2.1)	1.05 (0.68 to 1.62)		15 (2.2)	1.07 (0.61 to 1.85)	
	>613–2408	223 (2.3)	26 (2.2)	1.05 (0.68 to 1.62)		17 (2.5)	1.16 (0.68 to 1.98)	
	>2408	227 (2.3)	16 (1.4)	0.63 (0.37 to 1.07)		11 (1.6)	0.72 (0.38 to 1.37)	
Carbaryl§	Never	5720 (58.8)	605 (52.5)	Ref	0.9	341 (51.7)	Ref	0.96
	>0–341	1347 (13.9)	184 (16.0)	1.16 (0.97 to 1.39)		106 (16.1)	1.19 (0.94 to 1.50)	
	>341–2015	1351 (13.9)	204 (17.7)	1.33 (1.11 to 1.60)		116 (17.6)	1.30 (1.03 to 1.65)	
	>2015	1302 (13.4)	159 (13.8)	1.11 (0.88 to 1.39)		96 (14.6)	1.10 (0.83 to 1.46)	

continued

Table 3 continued

Pesticides	Exposure*	No OI (n (%))	Any OI† (n=20 409)			Time-restricted OI‡ (n=19 563)		
			OI (n (%))	OR (95% CI)	P trend	OI (n (%))	OR (95% CI)	P trend
Carbofuran	Never	12 129 (71.4)	1277 (66.0)	Ref	0.51	753 (65.8)	Ref	0.99
	>0–350	1600 (9.4)	239 (12.3)	1.27 (1.09 to 1.47)		134 (11.7)	1.20 (0.99 to 1.46)	
	>350–1260	1631 (9.6)	221 (11.4)	1.16 (1.00 to 1.36)		142 (12.4)	1.25 (1.03 to 1.50)	
	>1260	1616 (9.5)	199 (10.3)	1.06 (0.90 to 1.25)		115 (10.1)	0.99 (0.81 to 1.22)	
Organophosphate	Chlorpyrifos	Never	9449 (54.9)	1023 (51.9)	Ref	607 (52.2)	Ref	0.99
	>0–435	2532 (14.7)	344 (17.5)	1.26 (1.10 to 1.44)		199 (17.1)	1.25 (1.05 to 1.48)	
	>435–1715	2658 (15.4)	305 (15.5)	1.06 (0.93 to 1.22)		185 (15.9)	1.09 (0.92 to 1.30)	
	>1715	2573 (14.9)	299 (15.2)	1.07 (0.94 to 1.23)		172 (14.8)	1.04 (0.87 to 1.24)	
Coumaphos	Never	15 223 (90.6)	1693 (88.9)	Ref	0.99	1007 (89.6)	Ref	0.34
	>0–394	539 (3.2)	77 (4.0)	1.19 (0.93 to 1.53)		42 (3.7)	1.09 (0.79 to 1.51)	
	>394–1369	513 (3.1)	76 (4.0)	1.26 (0.98 to 1.61)		46 (4.1)	1.29 (0.94 to 1.76)	
	>1369	531 (3.2)	59 (3.1)	0.95 (0.72 to 1.26)		29 (2.6)	0.78 (0.53 to 1.15)	
Diazinon§	Never	7891 (79.4)	866 (72.9)	Ref	0.01	500 (73.2)	Ref	0.18
	>0–515	698 (7.0)	118 (9.9)	1.45 (1.17 to 1.79)		70 (10.2)	1.47 (1.12 to 1.92)	
	>515–3923	679 (6.8)	99 (8.3)	1.22 (0.97 to 1.54)		55 (8.1)	1.15 (0.85 to 1.55)	
	>3923	668 (6.7)	105 (8.8)	1.40 (1.11 to 1.76)		58 (8.5)	1.26 (0.93 to 1.70)	
Dichlorvos	Never	14 949 (87.8)	1630 (84.3)	Ref	0.08	974 (85.0)	Ref	0.06
	>0–315	691 (4.1)	93 (4.8)	1.15 (0.92 to 1.44)		47 (4.1)	1.00 (0.74 to 1.37)	
	>315–1143	697 (4.1)	111 (5.7)	1.33 (1.08 to 1.64)		64 (5.6)	1.33 (1.02 to 1.75)	
	>1143	684 (4.0)	99 (5.1)	1.22 (0.98 to 1.52)		61 (5.3)	1.29 (0.98 to 1.70)	
Fonofos	Never	13 149 (76.8)	1461 (75.0)	Ref	0.39	869 (75.4)	Ref	0.47
	>0–429	1289 (7.5)	183 (9.4)	1.19 (1.01 to 1.41)		105 (9.1)	1.19 (0.96 to 1.48)	
	>429–1550	1371 (8)	147 (7.5)	0.87 (0.72 to 1.04)		87 (7.6)	0.90 (0.71 to 1.13)	
	>1550	1310 (7.7)	158 (8.1)	0.95 (0.80 to 1.14)		91 (7.9)	0.94 (0.75 to 1.19)	
Malathion§	Never	3562 (34.8)	345 (28.3)	Ref	0.01	182 (26.0)	Ref	0.01
	>0–360	2215 (21.6)	281 (23.1)	1.24 (1.05 to 1.47)		165 (23.5)	1.44 (1.15 to 1.80)	
	>360–1344	2290 (22.4)	280 (23.0)	1.17 (0.98 to 1.38)		169 (24.1)	1.39 (1.11 to 1.74)	
	>1344	2172 (21.2)	311 (25.6)	1.33 (1.13 to 1.58)		185 (26.4)	1.50 (1.21 to 1.87)	
Parathion§	Never	9549 (93.1)	1099 (90.5)	Ref	0.23	638 (91.3)	Ref	0.54
	>0–315	232 (2.3)	41 (3.4)	1.41 (1.00 to 1.99)		23 (3.3)	1.32 (0.85 to 2.06)	
	>315–1700	239 (2.3)	40 (3.3)	1.39 (0.98 to 1.98)		18 (2.6)	1.01 (0.62 to 1.66)	
	>1700	237 (2.3)	34 (2.8)	1.22 (0.84 to 1.77)		20 (2.9)	1.17 (0.73 to 1.88)	
Phorate§	Never	6682 (67.8)	741 (63.6)	Ref	0.64	438 (65.1)	Ref	0.15
	>0–315	1082 (11)	148 (12.7)	1.09 (0.90 to 1.32)		82 (12.2)	1.05 (0.81 to 1.35)	
	>315–1117	1036 (10.5)	147 (12.6)	1.16 (0.96 to 1.41)		90 (13.4)	1.26 (0.99 to 1.61)	
	>1117	1057 (10.7)	130 (11.1)	0.95 (0.78 to 1.17)		63 (9.4)	0.80 (0.61 to 1.05)	

continued

Table 3 continued

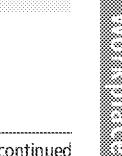
Pesticides	Exposure*	Any OI† (n=20 409)			Time-restricted OI‡ (n=19 563)		
		No OI (n (%))	OI (n (%))	OR (95% CI)	P trend	OI (n (%))	OR (95% CI)
Terbufos	Never	10 133 (59.3)	1099 (56.4)	Ref	0.07	652 (56.9)	Ref
	>0–621	2300 (13.5)	278 (14.3)	1.08 (0.94 to 1.25)		163 (14.2)	1.13 (0.94 to 1.35)
	>621–2279	2387 (14.0)	272 (14.0)	1.00 (0.87 to 1.16)		149 (13.0)	0.96 (0.79 to 1.16)
	>2279	2274 (13.3)	299 (15.3)	1.15 (1.00 to 1.33)		182 (15.9)	1.21 (1.01 to 1.44)
Permethrin	Permethrin (crops)	14 678 (86.7)	1625 (84.9)	Ref	0.001	962 (85)	Ref
	>0–245	744 (4.4)	94 (4.9)	1.15 (0.92 to 1.44)		54 (4.8)	1.15 (0.87 to 1.55)
	>245–963	779 (4.6)	89 (4.6)	1.09 (0.87 to 1.37)		46 (4.1)	0.99 (0.73 to 1.34)
	>963	726 (4.3)	106 (5.5)	1.42 (1.15 to 1.76)		70 (6.2)	1.55 (1.19 to 2.01)
Permethrin (animals)	Never	14 557 (84.9)	1610 (82.7)	Ref	0.38	950 (82.6)	Ref
	>0–350	845 (4.9)	125 (6.4)	1.39 (1.14 to 1.70)		73 (6.3)	1.48 (1.15 to 1.92)
	>350–1382	886 (5.2)	110 (5.6)	1.16 (0.94 to 1.43)		68 (5.9)	1.31 (1.01 to 1.70)
	>1382	866 (5.0)	102 (5.2)	1.10 (0.89 to 1.37)		59 (5.1)	1.15 (0.87 to 1.52)
Fumigant	CCl <sub>4</sub> /CS <sub>2</sub> §	9947 (96.2)	1146 (93.5)	Ref	0.11	651 (91.9)	Ref
	>0–63	129 (1.2)	27 (2.2)	1.44 (0.94 to 2.20)		19 (2.7)	1.83 (1.12 to 3.01)
	>63–331	136 (1.3)	26 (2.1)	1.22 (0.79 to 1.87)		18 (2.5)	1.48 (0.89 to 2.46)
	>331	125 (1.2)	27 (2.2)	1.40 (0.91 to 2.14)		20 (2.8)	1.80 (1.10 to 2.95)
Aluminium phosphide§	Never	9963 (96.3)	1181 (95.8)	Ref	0.67	681 (95.6)	Ref
	>0–56	124 (1.2)	21 (1.7)	1.37 (0.85 to 2.20)		14 (2.0)	1.68 (0.95 to 2.95)
	>56–248	128 (1.2)	18 (1.5)	1.16 (0.70 to 1.92)		9 (1.3)	1.05 (0.53 to 2.09)
	>248	130 (1.3)	13 (1.1)	0.84 (0.47 to 1.51)		8 (1.1)	0.93 (0.45 to 1.92)
Ethylene dibromide§	Never	9937 (96)	1182 (95.6)	Ref	0.56	679 (95.4)	Ref
	>0–196	138 (1.3)	18 (1.5)	1.15 (0.69 to 1.90)		7 (1.0)	0.77 (0.36 to 1.67)
	>196–919	137 (1.3)	19 (1.5)	1.24 (0.75 to 2.04)		12 (1.7)	1.31 (0.71 to 2.42)
	>919	135 (1.3)	18 (1.5)	1.14 (0.68 to 1.90)		14 (2.0)	1.45 (0.81 to 2.58)
Methyl bromide	Never	14 751 (86.6)	1673 (86.9)	Ref	0.55	971 (85.9)	Ref
	>0–294	740 (4.3)	81 (4.2)	1.01 (0.79 to 1.31)		50 (4.4)	1.00 (0.73 to 1.37)
	>294–1260	782 (4.6)	90 (4.7)	1.05 (0.81 to 1.36)		61 (5.4)	1.09 (0.80 to 1.48)
	>1260	765 (4.5)	81 (4.2)	0.93 (0.71 to 1.21)		49 (4.3)	0.83 (0.59 to 1.17)
Fungicide	Benomyl§	8915 (93.5)	1040 (92.3)	Ref	0.15	593 (91.7)	Ref
	>0–343	199 (2.1)	36 (3.2)	1.66 (1.13 to 2.43)		21 (3.2)	1.73 (1.07 to 2.81)
	>343–1773	220 (2.3)	20 (1.8)	0.87 (0.53 to 1.45)		12 (1.9)	0.95 (0.50 to 1.79)
	>1773	197 (2.1)	31 (2.8)	1.47 (0.94 to 2.28)		21 (3.2)	1.73 (1.02 to 2.95)
Captan	Never	14 920 (89.3)	1647 (86.9)	Ref	0.05	977 (86.5)	Ref
	>0–9	667 (4.0)	90 (4.7)	1.21 (0.96 to 1.53)		51 (4.5)	1.22 (0.91 to 1.64)
	>9–161	528 (3.2)	74 (3.9)	1.24 (0.96 to 1.59)		48 (4.3)	1.39 (1.02 to 1.89)
	>161	584 (3.5)	85 (4.5)	1.29 (1.02 to 1.64)		53 (4.7)	1.30 (0.97 to 1.75)

continued

Table 3 continued

Pesticides	Exposure*	No OI (n (%))	Any OI† (n=20 409)			Time-restricted OI‡ (n=19 563)		
			OI (n (%))	OR (95% CI)	P trend	OI (n (%))	OR (95% CI)	P trend
Chlorothalonil	Never	15 917 (93.7)	1788 (93.4)	Ref	0.94	1048 (92.6)	Ref	0.41
	>0–539	345 (2.0)	47 (2.5)	1.29 (0.93 to 1.78)		29 (2.6)	1.31 (0.88 to 1.95)	
	>539–3080	362 (2.1)	44 (2.3)	1.20 (0.85 to 1.69)		28 (2.5)	1.22 (0.80 to 1.87)	
	>3080	372 (2.2)	36 (1.9)	1.00 (0.69 to 1.46)		27 (2.4)	1.22 (0.79 to 1.89)	
Maneb/Mancozeb§	Never	9130 (93.1)	1086 (93.1)	Ref	0.82	618 (92.1)	Ref	0.58
	>0–425	232 (2.4)	22 (1.9)	0.81 (0.51 to 1.28)		14 (2.1)	0.89 (0.50 to 1.56)	
	>425–2688	232 (2.4)	30 (2.6)	1.05 (0.69 to 1.60)		20 (3.0)	1.20 (0.72 to 1.99)	
	>2688	216 (2.2)	28 (2.4)	1.03 (0.67 to 1.58)		19 (2.8)	1.14 (0.68 to 1.91)	
Metalaxyl§	Never	8425 (82.8)	995 (82.2)	Ref	0.14	573 (82.2)	Ref	0.64
	>0–239	578 (5.7)	73 (6.0)	1.07 (0.83 to 1.38)		41 (5.9)	1.03 (0.74 to 1.44)	
	>239–1323	599 (5.9)	69 (5.7)	1.13 (0.85 to 1.51)		41 (5.9)	1.06 (0.73 to 1.53)	
	>1323	577 (5.7)	73 (6.0)	1.28 (0.94 to 1.74)		42 (6.0)	1.11 (0.75 to 1.64)	
Herbicide								
Alachlor	Never	7629 (44.9)	794 (41.0)	Ref	0.08	478 (41.7)	Ref	0.19
	>0–788	3131 (18.4)	358 (18.5)	1.01 (0.88 to 1.16)		206 (18.0)	0.99 (0.84 to 1.18)	
	>788–2958	3153 (18.6)	391 (20.2)	1.10 (0.97 to 1.26)		228 (19.9)	1.09 (0.92 to 1.29)	
	>2958	3070 (18.1)	393 (20.3)	1.13 (0.99 to 1.29)		235 (20.5)	1.11 (0.94 to 1.32)	
Butylate§	Never	6975 (71.1)	790 (67.8)	Ref	0.17	462 (68.8)	Ref	0.31
	>0–455	949 (9.7)	126 (10.8)	1.08 (0.87 to 1.32)		73 (10.9)	1.08 (0.83 to 1.41)	
	>455–1512	974 (9.9)	117 (10.0)	0.96 (0.78 to 1.19)		60 (8.9)	0.86 (0.65 to 1.15)	
	>1512	916 (9.3)	133 (11.4)	1.17 (0.95 to 1.44)		77 (11.5)	1.18 (0.90 to 1.53)	
Chlorimuron ethyl§	Never	7021 (68.1)	828 (67.3)	Ref	0.58	485 (68.3)	Ref	0.62
	>0–236	1130 (11.0)	141 (11.5)	1.09 (0.90 to 1.32)		80 (11.3)	1.11 (0.86 to 1.42)	
	>236–662	1076 (10.4)	131 (10.7)	1.04 (0.85 to 1.26)		69 (9.7)	0.96 (0.74 to 1.26)	
	>662	1089 (10.6)	130 (10.6)	1.06 (0.87 to 1.30)		76 (10.7)	1.08 (0.84 to 1.40)	
Dicamba	Never	7694 (45.3)	793 (41.0)	Ref	0.68	493 (43.2)	Ref	0.95
	>0–551	3080 (18.1)	379 (19.6)	1.15 (1.00 to 1.33)		214 (18.8)	1.12 (0.93 to 1.35)	
	>551–2170	3166 (18.6)	396 (20.5)	1.14 (0.99 to 1.32)		229 (20.1)	1.13 (0.94 to 1.36)	
	>2170	3063 (18.0)	366 (18.9)	1.09 (0.94 to 1.26)		205 (18.0)	1.04 (0.87 to 1.26)	
EPTC	Never	13 352 (78.9)	1487 (77.3)	Ref	0.38	889 (77.9)	Ref	0.55
	>0–315	1212 (7.2)	132 (6.9)	0.93 (0.77 to 1.12)		77 (6.7)	0.95 (0.75 to 1.22)	
	>315–1176	1217 (7.2)	160 (8.3)	1.12 (0.94 to 1.34)		93 (8.2)	1.13 (0.90 to 1.42)	
	>1176	1147 (6.8)	144 (7.5)	1.07 (0.89 to 1.28)		82 (7.2)	1.06 (0.83 to 1.34)	
Glyphosate	Never	4163 (23.0)	381 (18.6)	Ref	0	226 (18.7)	Ref	0.02
	>0–672	4590 (25.4)	573 (28)	1.38 (1.21 to 1.59)		340 (28.1)	1.39 (1.16 to 1.65)	
	>672–2610	4748 (26.3)	523 (25.6)	1.22 (1.06 to 1.41)		302 (25.0)	1.17 (0.98 to 1.41)	
	>2610	4572 (25.3)	567 (27.7)	1.41 (1.22 to 1.62)		342 (28.3)	1.40 (1.17 to 1.68)	

continued

**Table 3** continued

Pesticides	Exposure*	No OI (n (%))	Any OI (n=20 409)			Time-restricted OI‡ (n=19 563)		
			OI (n (%))	OR (95% CI)	P trend	OI (n (%))	OR (95% CI)	P trend
Imazethapyr	Never	8934 (53.6)	1000 (52.9)	Ref	0.65	611 (54.8)	Ref	0.86
	>0–338	2545 (15.3)	310 (16.4)	1.00 (0.86 to 1.16)		172 (15.4)	0.97 (0.80 to 1.18)	
	>338–992	2677 (16.1)	287 (15.2)	0.88 (0.76 to 1.03)		163 (14.6)	0.88 (0.72 to 1.07)	
	>992	2519 (15.1)	294 (15.5)	0.97 (0.83 to 1.13)		168 (15.1)	0.98 (0.80 to 1.19)	
Metolachlor	Never	8916 (52.2)	988 (50.6)	Ref	0.05	586 (50.5)	Ref	0.21
	>0–720	2704 (15.8)	367 (18.8)	1.20 (1.05 to 1.36)		217 (18.7)	1.25 (1.05 to 1.47)	
	>720–2604	2756 (16.1)	315 (16.1)	0.99 (0.86 to 1.14)		191 (16.5)	1.06 (0.89 to 1.26)	
	>2604	2693 (15.8)	282 (14.4)	0.91 (0.79 to 1.05)		166 (14.3)	0.94 (0.78 to 1.13)	
Paraquat§	Never	8817 (85.4)	1022 (83.2)	Ref	0.11	589 (83.1)	Ref	0.09
	>0–275	501 (4.9)	68 (5.5)	1.17 (0.90 to 1.53)		38 (5.4)	1.14 (0.80 to 1.61)	
	>275–1080	507 (4.9)	72 (5.9)	1.29 (0.98 to 1.68)		40 (5.6)	1.24 (0.88 to 1.76)	
	>1080	498 (4.8)	66 (5.4)	1.27 (0.95 to 1.70)		42 (5.9)	1.38 (0.96 to 1.97)	
Pendimethalin§	Never	6521 (63.2)	755 (61.3)	Ref	0.55	440 (62.1)	Ref	0.73
	>0–315	1282 (12.4)	154 (12.5)	1.01 (0.84 to 1.21)		92 (13.0)	1.06 (0.83 to 1.34)	
	>315–1176	1250 (12.1)	180 (14.6)	1.28 (1.07 to 1.53)		94 (13.3)	1.18 (0.93 to 1.49)	
	>1176	1264 (12.3)	143 (11.6)	1.03 (0.85 to 1.25)		82 (11.6)	1.03 (0.80 to 1.33)	
Petroleum distillates§	Never	8058 (78.7)	911 (74.1)	Ref	0.03	530 (74.6)	Ref	0.05
	>0–502	733 (7.2)	100 (8.1)	1.18 (0.94 to 1.47)		55 (7.7)	1.15 (0.86 to 1.54)	
	>502–2438	734 (7.2)	112 (9.1)	1.34 (1.09 to 1.67)		63 (8.9)	1.35 (1.02 to 1.78)	
	>2438	717 (7.0)	106 (8.6)	1.27 (1.02 to 1.58)		62 (8.7)	1.31 (0.99 to 1.74)	
Trifluralin	Never	7297 (45.1)	742 (40.5)	Ref	0.11	453 (42.2)	Ref	0.16
	>0–1020	2960 (18.3)	331 (18.1)	1.02 (0.88 to 1.19)		180 (16.8)	0.95 (0.78 to 1.15)	
	>1020–3875	3030 (18.7)	377 (20.6)	1.11 (0.95 to 1.28)		216 (20.1)	1.07 (0.89 to 1.29)	
	>3875	2897 (17.9)	382 (20.9)	1.13 (0.98 to 1.32)		225 (20.9)	1.12 (0.92 to 1.35)	
2,4-D	Never	4001 (22.3)	364 (17.9)	Ref	0.05	225 (18.8)	Ref	0.26
	>0–1302	4646 (25.9)	516 (25.4)	1.14 (0.98 to 1.31)		312 (26.0)	1.16 (0.96 to 1.39)	
	>1302–5208	4858 (27.0)	548 (27.0)	1.08 (0.93 to 1.26)		309 (25.8)	1.03 (0.85 to 1.24)	
	>5208	4459 (24.8)	600 (29.6)	1.20 (1.03 to 1.39)		354 (29.5)	1.16 (0.96 to 1.40)	
2,4,5-T§	Never	7999 (82.2)	828 (71.6)	Ref	0.05	472 (70.9)	Ref	0.23
	>0–280	568 (5.8)	116 (10.0)	1.64 (1.32 to 2.05)		74 (11.1)	1.82 (1.38 to 2.38)	
	>280–971	586 (6.0)	117 (10.1)	1.65 (1.32 to 2.07)		65 (9.8)	1.56 (1.17 to 2.08)	
	>971	579 (5.9)	95 (8.2)	1.33 (1.05 to 1.70)		55 (8.3)	1.29 (0.95 to 1.75)	
2,4,5-TP§	Never	9291 (95.3)	1071 (92.5)	Ref	0.25	621 (93.1)	Ref	0.72
	>0–315	159 (1.6)	26 (2.2)	1.16 (0.75 to 1.79)		15 (2.2)	1.12 (0.64 to 1.94)	
	>315–1250	148 (1.5)	35 (3.0)	1.66 (1.13 to 2.44)		20 (3.0)	1.62 (0.99 to 2.64)	
	>1250	148 (1.5)	26 (2.2)	1.20 (0.78 to 1.85)		11 (1.6)	0.82 (0.44 to 1.54)	
Atrazine	Never	4859 (26.9)	473 (23.2)	Ref	0.5	286 (23.7)	Ref	0.55
	>0–1054	4386 (24.2)	509 (25.0)	1.12 (0.98 to 1.29)		300 (24.9)	1.15 (0.96 to 1.37)	
	>1054–4340	4530 (25.0)	523 (25.7)	1.07 (0.93 to 1.23)		302 (25.0)	1.06 (0.89 to 1.27)	
	>4340	4318 (23.9)	531 (26.1)	1.10 (0.96 to 1.27)		318 (26.4)	1.12 (0.94 to 1.34)	

continued

Table 3 continued

Pesticides	Exposure*	Any Olf† (n=20 409)			Time-restricted Olf‡ (n=19 563)			
		No Olf (n (%))	Olf (n (%))	OR (95% CI)	p trend	Olf (n (%))	OR (95% CI)	p trend
Cyanazine	Never	9485 (55.6)	1007 (51.7)	Ref	0.33	594 (51.6)	Ref	0.56
	>0-539	2503 (14.7)	321 (16.5)	1.12 (0.97 to 1.29)		189 (16.4)	1.20 (1.00 to 1.43)	
	>539-2200	2592 (15.2)	301 (15.5)	1.09 (0.86 to 1.15)		190 (16.5)	1.13 (0.95 to 1.36)	
	>2200	2490 (14.6)	318 (16.3)	1.10 (0.95 to 1.27)		178 (15.5)	1.11 (0.92 to 1.33)	
Metribuzin§	Never	5550 (58.3)	605 (53.6)	Ref	0.02	359 (55.1)	Ref	0.37
	>0-315	1323 (13.9)	156 (13.8)	0.99 (0.81 to 1.21)		100 (15.4)	1.14 (0.88 to 1.46)	
	>315-1000	1361 (14.3)	176 (15.6)	1.10 (0.91 to 1.34)		93 (14.3)	1.04 (0.81 to 1.35)	
	>1000	1286 (13.5)	191 (16.9)	1.24 (1.02 to 1.50)		99 (15.2)	1.15 (0.89 to 1.48)	

as changes in pesticide exposures resulting from the regulatory and usage pattern changes.

Despite the limitations, ours is the first study that has comprehensively evaluated exposures to overall and specific pesticides in relation to olfactory function among older adults. Notably, we asked about sense of smell 19 years after exposure assessment, and thus the results could not be readily explained by reverse causation. Further, we analysed both overall and specific pesticide use in relation to olfactory impairment among farmers who have been shown to provide reliable and valid information on pesticide exposures.<sup>38,39</sup> Future studies need to confirm our findings with objectively assessed sense of smell.

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**Data availability statement** Requests for data, including the data used in this manuscript, are welcome as described on the Study Website (<https://www.aghealth.nih.gov/collaboration/process.html>). Data requests may be made directly at [www.aghealthstars.com](http://www.aghealthstars.com); registration is required. The Agricultural Health Study is an ongoing prospective study. The data sharing policy was developed to protect the privacy of study participants and is consistent with study informed consent documents as approved by the NIH Institutional Review Board. Dr Dale Sandler is the NIEHS Principal Investigator of the Agricultural Health Study and is responsible for ensuring participant safety and privacy.

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**Supplementary table 1: Characteristics of participants those who returned vs. those who did not return the take-home questionnaire at enrollment in the Agricultural Health Study (n=20,409), Iowa and North Carolina**

Characteristics	Returned take home	
	No (n=29478)	Yes (n=22916)
Age (years)		
≤45	16070 (54.5)	9657 (42.1)
>45-55	6600 (22.4)	5244 (22.9)
>55-65	4549 (15.4)	5059 (22.1)
>65	2259 (7.7)	2956 (12.9)
Sex		
Female	803 (2.7)	556 (2.4)
Male	28675 (97.3)	22360 (97.6)
Race		
Other	1090 (3.7)	428 (1.9)
White	27853 (94.5)	21986 (95.9)
Missing	535 (1.8)	502 (2.2)
State		
Iowa	17066 (57.9)	14810 (64.6)
North Carolina	12412 (42.1)	8106 (35.4)
Marital status		
Never married	3153 (10.7)	2365 (10.3)
Married/Living as married	24472 (83.0)	19220 (83.9)
Divorced/Widowed	1715 (5.8)	1209 (5.3)
Missing	138 (0.5)	122 (0.5)
Education		
≤ High school	16638 (56.4)	12647 (55.2)
1-3 year beyond high school	6946 (23.6)	5173 (22.6)
≥ College graduate	4588 (15.6)	4001 (17.5)
Something else	69 (0.2)	48 (0.2)
Missing	1237 (4.2)	1047 (4.6)
Smoking status		
Never	14961 (50.8)	11974 (52.3)
Former	8422 (28.6)	7568 (33)
Current	5265 (17.9)	2922 (12.8)
Missing	830 (2.8)	452 (2.0)
Alcohol intake (past 12 months)		
No	8976 (30.4)	7869 (34.3)
Yes	18152 (61.6)	13813 (60.3)
Missing	2350 (8.0)	1234 (5.4)
Overall pesticide lifetime days		
0-64	8740 (29.6)	6535 (28.5)
>64-225	8664 (29.4)	7181 (31.3)
>225-458	5856 (19.9)	4660 (20.3)
>458	5568 (18.9)	4514 (19.7)
Missing	650 (2.2)	26 (0.1)

**Supplementary table 2:** Ever-use of pesticide at enrollment in relation to self-reported olfactory impairment reported in the third follow-up in the Agricultural Health Study, excluding head injury

Pesticides	Those who returned the take home and those responded to the head injury question (n=10,162) <sup>a</sup>	
	OI (n=1048), n(%)	OR (95% CI)
Insecticide	1022 (97.5)	1.39 (0.92, 2.10)
Organochlorine	721 (69.1)	1.21 (1.04, 1.41)
Aldrin	282 (29.4)	1.01 (0.83, 1.24)
Chlordane	376 (38.1)	1.27 (1.09, 1.49)
Dieldrin	121 (12.6)	1.20 (0.94, 1.53)
DDT	362 (36.9)	1.13 (0.95, 1.35)
Heptachlor	251 (26.1)	1.10 (0.90, 1.35)
Toxaphene	201 (20.5)	1.24 (1.04, 1.48)
Lindane	268 (27.1)	1.19 (1.02, 1.39)
Carbamate	808 (77.2)	1.37 (1.17, 1.61)
Aldicarb	74 (7.6)	0.80 (0.60, 1.06)
Carbaryl	615 (62.9)	1.15 (0.98, 1.34)
Carbofuran	347 (35.0)	1.17 (1.01, 1.35)
Organophosphate	997 (95.2)	1.54 (1.14, 2.08)
Chlorpyrifos	498 (47.9)	1.25 (1.10, 1.43)
Coumaphos	113 (11.6)	1.13 (0.91, 1.39)
Diazinon	373 (38.1)	1.11 (0.95, 1.29)
Dichlorvos	159 (16.0)	1.19 (0.98, 1.43)
Fonofos	256 (25.6)	1.03 (0.88, 1.21)
Malathion	817 (80.1)	1.34 (1.13, 1.58)
Parathion	180 (18.4)	1.16 (0.97, 1.39)
Phorate	386 (39.1)	1.02 (0.88, 1.18)
Terbufos	434 (43.3)	1.08 (0.94, 1.24)
Trichlorfon	7 (0.7)	1.22 (0.55, 2.73)
Permethrin (crops)	150 (15.2)	1.27 (1.05, 1.54)
Permethrin (animals)	169 (16.9)	1.30 (1.08, 1.57)
Fumigant	283 (27.0)	1.19 (1.01, 1.39)
CCl <sub>4</sub> /CS <sub>2</sub>	96 (9.8)	1.36 (1.07, 1.73)
Aluminum phosphide	59 (6.0)	1.18 (0.89, 1.57)
Ethylene dibromide	33 (3.3)	0.91 (0.62, 1.32)
Methyl bromide	124 (12.5)	0.88 (0.68, 1.14)
Fungicide	389 (37.2)	1.12 (0.97, 1.31)
Benomyl	93 (9.7)	1.30 (0.97, 1.76)
Captan	130 (13.1)	1.17 (0.95, 1.42)
Chlorothalonil	59 (6)	0.94 (0.68, 1.30)
Maneb	87 (8.9)	0.85 (0.64, 1.14)
Metalaxyl	216 (21.8)	1.18 (0.98, 1.43)
Ziram	17 (1.7)	1.23 (0.73, 2.07)
Herbicide	1033 (98.6)	1.07 (0.62, 1.86)
Alachlor	615 (61.6)	1.15 (1.00, 1.32)
Butylate	372 (38.0)	1.05 (0.91, 1.23)
Chlorimuron ethyl	370 (37.6)	1.05 (0.91, 1.21)
Dicamba	592 (59.4)	1.12 (0.95, 1.31)
EPTC	226 (22.9)	1.05 (0.89, 1.24)
Glyphosate	857 (82.2)	1.33 (1.12, 1.58)
Imazethapyr	457 (47.1)	0.96 (0.82, 1.13)

Metolachlor	502 (50.0)	1.04 (0.90, 1.19)
Paraquat	230 (23.4)	1.10 (0.92, 1.30)
Pendimethalin	442 (44.7)	1.08 (0.94, 1.24)
Petroleum distillates	543 (55.1)	1.21 (1.05, 1.39)
Trifluralin	557 (58.9)	1.04 (0.88, 1.22)
2,4-D	868 (83.4)	1.16 (0.97, 1.40)
2,4,5-T	305 (31.2)	1.25 (1.05, 1.48)
2,4,5-TP	105 (10.7)	0.72 (0.57, 0.92)
Atrazine	808 (77.8)	1.17 (0.99, 1.39)
Cyanazine	495 (49.5)	1.14 (0.98, 1.31)
Metribuzin	510 (53.3)	1.03 (0.88, 1.22)

Abbreviation: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; 2,4,5-T,P, 2-(2,4,5-trichlorophenoxy) propionic acid; CI, Confidence Intervals; CCl<sub>4</sub>/CS<sub>2</sub>, Carbon tetrachloride/Carbon disulfide 80/20 mix; DDT, Dichlorodiphenyltrichloroethane; EPTC, S-Ethyl dipropylthiocarbamate; OI, Olfactory Impairment; OR, Odds Ratio

Odds ratios are adjusted for age, sex, state of residence, education, smoking status, ever performed following tasks at least once each year (repair engines, replace asbestos brake linings, handle stored grain, work in swine confinement areas, weld and paint), and correlated pesticides (correlated ever-use of pesticides with Spearman correlation  $\geq 0.40$ )

<sup>a</sup>Restricted to participants who returned the take-home questionnaire and those who responded to the question on a history of head injury; those with a history of head injury were excluded

**Supplementary table 3:** Ever-use of pesticide at enrollment in relation to self-reported olfactory impairment reported in the third follow-up in the Agricultural Health Study, excluding those who reported PD in any survey (n=20,184)

Pesticides	No OI n (%)	OI n (%)	OR (95% CI)
Insecticide	17161 (94.1)	1873 (96.2)	1.42 (1.11, 1.82)
Organochlorine	9642 (54.4)	1246 (65.4)	1.29 (1.15, 1.44)
Aldrin	3226 (19.4)	467 (26.5)	1.01 (0.87, 1.18)
Chlordane	4464 (26.4)	605 (33.3)	1.08 (0.96, 1.22)
Dieldrin	1150 (6.9)	199 (11.3)	1.23 (1.02, 1.48)
DDT	3918 (23.3)	612 (34.0)	1.28 (1.13, 1.47)
Heptachlor	2795 (16.7)	411 (23.2)	1.07 (0.92, 1.25)
Toxaphene	2400 (14.2)	346 (19.2)	1.23 (1.08, 1.40)
Lindane	3639 (21.5)	490 (26.9)	1.20 (1.07, 1.34)
Carbamate	12163 (67.9)	1448 (75.5)	1.40 (1.25, 1.57)
Aldicarb	1686 (10.1)	164 (9.2)	0.93 (0.77, 1.13)
Carbaryl	9554 (56.4)	1138 (62.6)	1.24 (1.10, 1.39)
Carbofuran	4941 (29.0)	629 (34.3)	1.16 (1.05, 1.29)
Organophosphate	16413 (90.0)	1823 (93.7)	1.51 (1.24, 1.84)
Chlorpyrifos	7840 (43.3)	910 (47.0)	1.16 (1.05, 1.27)
Coumaphos	1621 (9.7)	205 (11.4)	1.14 (0.98, 1.33)
Diazinon	5615 (33.2)	671 (36.9)	1.04 (0.93, 1.17)
Dichlorvos	2102 (12.4)	291 (15.9)	1.24 (1.08, 1.43)
Fonofos	4033 (23.5)	467 (25.3)	1.00 (0.89, 1.13)
Malathion	12669 (72.8)	1488 (79.1)	1.31 (1.16, 1.48)
Parathion	2541 (15.1)	342 (18.9)	1.22 (1.07, 1.39)
Phorate	5972 (35.2)	691 (38.0)	1.00 (0.90, 1.11)
Terbufos	7070 (41.2)	806 (43.6)	1.06 (0.96, 1.17)
Trichlorfon	103 (0.6)	16 (0.9)	1.40 (0.82, 2.38)
Permethrin (crops)	2321 (13.7)	289 (15.9)	1.23 (1.08, 1.41)
Permethrin (animals)	2618 (15.3)	330 (18.0)	1.25 (1.10, 1.43)
Fumigant	4173 (22.9)	504 (25.9)	1.16 (1.03, 1.31)
CCl <sub>4</sub> /CS <sub>2</sub>	947 (5.6)	160 (8.9)	1.30 (1.09, 1.56)
Aluminum phosphide	910 (5.4)	106 (5.9)	1.06 (0.86, 1.31)
Ethylene dibromide	618 (3.7)	64 (3.5)	0.89 (0.68, 1.17)
Methyl bromide	2386 (14.0)	245 (13.5)	0.97 (0.81, 1.17)
Fungicide	6486 (35.6)	732 (37.7)	1.17 (1.05, 1.30)
Benomyl	1506 (9.1)	170 (9.6)	1.03 (0.83, 1.29)
Captan	2074 (12.2)	276 (15.1)	1.24 (1.08, 1.43)
Chlorothalonil	1148 (6.8)	137 (7.5)	1.23 (0.99, 1.54)
Maneb	1516 (8.9)	177 (9.8)	1.10 (0.89, 1.35)
Metalaxyl	3733 (21.9)	414 (22.8)	1.16 (1.01, 1.33)
Ziram	252 (1.5)	28 (1.6)	1.04 (0.70, 1.55)
Herbicide	17812 (97.7)	1915 (98.4)	1.26 (0.86, 1.84)
Alachlor	9593 (55.8)	1083 (58.9)	1.05 (0.95, 1.16)
Butylate	5746 (34.1)	680 (37.7)	1.04 (0.93, 1.17)
Chlorimuron ethyl	6451 (37.9)	690 (38.1)	1.00 (0.90, 1.10)
Dicamba	9460 (55.2)	1083 (59.1)	1.11 (0.99, 1.24)
EPTC	3648 (21.5)	430 (23.6)	1.07 (0.95, 1.21)
Glyphosate	14004 (77.2)	1585 (81.8)	1.36 (1.20, 1.54)
Imazethapyr	7860 (46.9)	852 (47.6)	0.94 (0.84, 1.06)
Metolachlor	8304 (48.3)	928 (50.1)	1.04 (0.94, 1.15)
Paraquat	3884 (22.8)	456 (25.1)	1.16 (1.03, 1.32)

Pendimethalin	7626 (44.7)	838 (46.0)	1.05 (0.95, 1.15)
Petroleum distillates	8441 (49.9)	1011 (55.7)	1.18 (1.06, 1.30)
Trifluralin	9047 (55.4)	1047 (60.0)	1.09 (0.96, 1.23)
2,4-D	14095 (78.0)	1589 (82.1)	1.14 (1.00, 1.30)
2,4,5-T	3707 (22.1)	520 (28.9)	1.21 (1.06, 1.38)
2,4,5-T,P	1658 (9.9)	209 (11.6)	0.89 (0.75, 1.07)
Atrazine	13327 (73.4)	1484 (76.9)	1.10 (0.97, 1.24)
Cyanazine	7714 (45.0)	887 (48.2)	1.05 (0.94, 1.17)
Metribuzin	8049 (49.0)	948 (53.8)	1.06 (0.94, 1.20)

Abbreviation: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; 2,4,5-T,P, 2-(2,4,5-trichlorophenoxy) propionic acid; CI, Confidence Intervals; CCl<sub>4</sub>/CS<sub>2</sub>, Carbon tetrachloride/Carbon disulfide 80/20 mix; DDT, Dichlorodiphenyltrichloroethane; EPTC, S-Ethyl dipropylthiocarbamate; OI, Olfactory Impairment; OR, Odds Ratio

Odds ratios are adjusted for age, sex, state of residence, education, smoking status, ever performed following tasks at least once each year (repair engines, replace asbestos brake linings, handle stored grain, work in swine confinement areas, weld and paint), and correlated pesticides (correlated ever-use of pesticides with Spearman correlation  $\geq 0.40$ )

**Supplementary table 4: Intensity-weighted lifetime days of use at enrollment in relation to self-reported olfactory impairment in the Agricultural Health Study, excluding those who reported PD in any survey (n=20,184)**

Pesticide	Exposure <sup>a</sup>	No OI (n (%))	OI (n (%))	OR (95% CI)	p-trend
<b>Organochlorine</b>					
Aldrin <sup>b</sup>	Never	8036 (83.9)	793 (75.8)	Ref	0.07
	>0–315	563 (5.9)	88 (8.4)	1.12 (0.87, 1.45)	
	>315–952	486 (5.1)	69 (6.6)	1.00 (0.75, 1.34)	
	>952	496 (5.2)	96 (9.2)	1.29 (0.99, 1.68)	
Chlordane <sup>b</sup>	Never	8030 (82)	806 (73.8)	Ref	0.10
	>0–231	577 (5.9)	97 (8.9)	1.41 (1.11, 1.78)	
	>231–637	606 (6.2)	95 (8.7)	1.27 (1.00, 1.61)	
	>637	583 (6.0)	94 (8.6)	1.23 (0.96, 1.56)	
Dieldrin <sup>b</sup>	Never	9316 (96.7)	1002 (94.7)	Ref	0.85
	>0–210	112 (1.2)	17 (1.6)	0.92 (0.55, 1.57)	
	>210–653	93 (1.0)	23 (2.2)	1.47 (0.91, 2.36)	
	>653	109 (1.1)	16 (1.5)	0.87 (0.51, 1.50)	
DDT <sup>b</sup>	Never	7838 (81.4)	743 (69.9)	Ref	0.01
	>0–328	598 (6.2)	107 (10.1)	1.38 (1.09, 1.75)	
	>328–1583	611 (6.3)	99 (9.3)	1.26 (0.98, 1.61)	
	>1583	587 (6.1)	114 (10.7)	1.46 (1.15, 1.85)	
Heptachlor <sup>b</sup>	Never	8490 (88.1)	872 (82.4)	Ref	0.15
	>0–289	394 (4.1)	55 (5.2)	1.01 (0.74, 1.37)	
	>289–893	382 (4.0)	65 (6.1)	1.20 (0.90, 1.61)	
	>893	368 (3.8)	66 (6.2)	1.22 (0.91, 1.64)	
Toxaphene <sup>b</sup>	Never	9247 (90.1)	977 (85.6)	Ref	0.19
	>0–298	340 (3.3)	51 (4.5)	1.24 (0.91, 1.68)	
	>298–1050	335 (3.3)	65 (5.7)	1.57 (1.19, 2.08)	
	>1050	342 (3.3)	48 (4.2)	1.15 (0.84, 1.58)	
Lindane <sup>b</sup>	Never	8730 (85.6)	890 (78.2)	Ref	<.0001
	>0–315	509 (5.0)	81 (7.1)	1.40 (1.09, 1.79)	
	>315–1176	493 (4.8)	77 (6.8)	1.41 (1.09, 1.82)	
	>1176	469 (4.6)	90 (7.9)	1.69 (1.32, 2.15)	
<b>Carbamate</b>					
Aldicarb <sup>b</sup>	Never	9122 (93.2)	1022 (93.9)	Ref	0.14
	>0–613	213 (2.2)	25 (2.3)	1.11 (0.72, 1.71)	
	>613–2408	221 (2.3)	25 (2.3)	1.07 (0.69, 1.68)	
	>2408	227 (2.3)	16 (1.5)	0.66 (0.39, 1.14)	
Carbaryl <sup>b</sup>	Never	5688 (58.9)	560 (52.1)	Ref	0.60
	>0–341	1340 (13.9)	172 (16.0)	1.19 (0.99, 1.43)	
	>341–2015	1345 (13.9)	191 (17.8)	1.37 (1.13, 1.65)	
	>2015	1292 (13.4)	151 (14.1)	1.17 (0.93, 1.47)	
Carbofuran	Never	12078 (71.5)	1203 (66.1)	Ref	0.31
	>0–350	1591 (9.4)	225 (12.4)	1.28 (1.09, 1.49)	
	>350–1260	1615 (9.6)	200 (11.0)	1.14 (0.97, 1.33)	
	>1260	1607 (9.5)	192 (10.5)	1.10 (0.93, 1.30)	
<b>Organophosphate</b>					
Chlorpyrifos	Never	9399 (54.9)	959 (51.7)	Ref	0.51
	>0–435	2520 (14.7)	326 (17.6)	1.27 (1.11, 1.46)	
	>435–1715	2646 (15.5)	290 (15.6)	1.08 (0.94, 1.24)	
	>1715	2554 (14.9)	280 (15.1)	1.07 (0.93, 1.24)	
Coumaphos	Never	15153 (90.6)	1595 (89.1)	Ref	0.89

	>0–394	535 (3.2)	70 (3.9)	1.17 (0.90, 1.51)	
	>394–1369	507 (3.0)	70 (3.9)	1.25 (0.97, 1.62)	
	>1369	531 (3.2)	55 (3.1)	0.94 (0.71, 1.25)	
Diazinon <sup>b</sup>	Never	7848 (79.4)	807 (72.7)	Ref	0.004
	>0–515	693 (7.0)	110 (9.9)	1.44 (1.16, 1.80)	
	>515–3923	675 (6.8)	93 (8.4)	1.23 (0.97, 1.56)	
	>3923	664 (6.7)	100 (9.0)	1.42 (1.12, 1.80)	
Dichlorvos	Never	14885 (87.9)	1533 (84.3)	Ref	0.04
	>0–315	688 (4.1)	89 (4.9)	1.18 (0.94, 1.49)	
	>315–1143	688 (4.1)	103 (5.7)	1.34 (1.08, 1.67)	
	>1143	677 (4.0)	93 (5.1)	1.24 (0.99, 1.55)	
Fonofos	Never	13085 (76.8)	1375 (75.0)	Ref	0.61
	>0–429	1282 (7.5)	177 (9.7)	1.24 (1.04, 1.47)	
	>429–1550	1364 (8.0)	133 (7.3)	0.85 (0.70, 1.03)	
	>1550	1303 (7.6)	148 (8.1)	0.96 (0.80, 1.15)	
Malathion <sup>b</sup>	Never	3541 (34.8)	315 (27.8)	Ref	0.001
	>0–360	2207 (21.7)	262 (23.1)	1.28 (1.07, 1.52)	
	>360–1344	2273 (22.3)	262 (23.1)	1.21 (1.01, 1.45)	
	>1344	2157 (21.2)	296 (26.1)	1.40 (1.18, 1.67)	
Parathion <sup>b</sup>	Never	9491 (93.1)	1022 (90.4)	Ref	0.07
	>0–315	232 (2.3)	38 (3.4)	1.41 (0.99, 2.01)	
	>315–1700	238 (2.3)	37 (3.3)	1.39 (0.97, 2.00)	
	>1700	236 (2.3)	34 (3.0)	1.31 (0.90, 1.90)	
Phorate <sup>b</sup>	Never	6643 (67.8)	693 (63.8)	Ref	0.81
	>0–315	1078 (11.0)	140 (12.9)	1.11 (0.91, 1.36)	
	>315–1117	1028 (10.5)	134 (12.3)	1.15 (0.94, 1.41)	
	>1117	1053 (10.7)	120 (11.0)	0.95 (0.77, 1.17)	
Terbufos	Never	10080 (59.3)	1041 (56.8)	Ref	0.04
	>0–621	2293 (13.5)	261 (14.2)	1.07 (0.93, 1.25)	
	>621–2279	2371 (13.9)	251 (13.7)	0.99 (0.85, 1.15)	
	>2279	2264 (13.3)	281 (15.3)	1.15 (0.99, 1.32)	
Permethrin					
Permethrin (crops)	Never	14601 (86.7)	1523 (84.7)	Ref	0.0006
	>0–245	742 (4.4)	90 (5.0)	1.16 (0.93, 1.46)	
	>245–963	778 (4.6)	82 (4.6)	1.06 (0.84, 1.35)	
	>963	725 (4.3)	104 (5.8)	1.47 (1.18, 1.82)	
Permethrin (animals)	Never	14491 (84.9)	1507 (82.3)	Ref	0.36
	>0–350	838 (4.9)	121 (6.6)	1.44 (1.18, 1.77)	
	>350–1382	880 (5.2)	108 (5.9)	1.22 (0.98, 1.50)	
	>1382	861 (5.0)	96 (5.2)	1.11 (0.89, 1.38)	
Fumigant					
CCl <sub>4</sub> /CS <sub>2</sub> <sup>b</sup>	Never	9891 (96.3)	1067 (93.3)	Ref	0.04
	>0–63	126 (1.2)	25 (2.2)	1.48 (0.96, 2.30)	
	>63–331	135 (1.3)	25 (2.2)	1.28 (0.83, 1.99)	
	>331	124 (1.2)	27 (2.4)	1.53 (0.99, 2.35)	
Aluminum phosphide <sup>b</sup>	Never	9904 (96.3)	1101 (95.7)	Ref	0.91
	>0–56	124 (1.2)	18 (1.6)	1.27 (0.77, 2.10)	
	>56–248	127 (1.2)	18 (1.6)	1.25 (0.76, 2.07)	
	>248	128 (1.2)	13 (1.1)	0.92 (0.51, 1.64)	
Ethylene dibromide <sup>b</sup>	Never	9877 (96)	1101 (95.5)	Ref	0.41
	>0–196	137 (1.3)	16 (1.4)	1.09 (0.64, 1.85)	

Methyl bromide	>196–919	136 (1.3)	18 (1.6)	1.26 (0.76, 2.09)	
	>919	135 (1.3)	18 (1.6)	1.21 (0.72, 2.02)	
	Never	14670 (86.6)	1574 (86.8)	Ref	0.71
	>0–294	738 (4.4)	74 (4.1)	0.97 (0.75, 1.27)	
	>294–1260	775 (4.6)	86 (4.7)	1.06 (0.82, 1.38)	
	>1260	765 (4.5)	79 (4.4)	0.95 (0.72, 1.25)	
Fungicide					
Benomyl <sup>b</sup>	Never	8866 (93.5)	967 (92.2)	Ref	0.13
	>0–343	198 (2.1)	34 (3.2)	1.68 (1.13, 2.49)	
	>343–1773	220 (2.3)	19 (1.8)	0.89 (0.53, 1.49)	
	>1773	194 (2.0)	29 (2.8)	1.51 (0.96, 2.37)	
Captan	Never	14849 (89.3)	1547 (86.7)	Ref	0.07
	>0–9	664 (4.0)	85 (4.8)	1.23 (0.97, 1.55)	
	>9–161	527 (3.2)	74 (4.1)	1.31 (1.02, 1.69)	
	>161	579 (3.5)	79 (4.4)	1.28 (1.00, 1.64)	
Chlorothalonil	Never	15833 (93.6)	1680 (93.2)	Ref	0.94
	>0–539	344 (2.0)	45 (2.5)	1.28 (0.92, 1.78)	
	>539–3080	358 (2.1)	42 (2.3)	1.20 (0.85, 1.71)	
	>3080	372 (2.2)	35 (1.9)	1.00 (0.68, 1.47)	
Maneb/Mancozeb <sup>b</sup>	Never	9078 (93.1)	1012 (93.2)	Ref	0.79
	>0–425	232 (2.4)	22 (2.0)	0.85 (0.54, 1.35)	
	>425–2688	230 (2.4)	25 (2.3)	0.93 (0.59, 1.46)	
	>2688	215 (2.2)	27 (2.5)	1.05 (0.68, 1.62)	
Metalaxyll <sup>b</sup>	Never	8370 (82.7)	926 (82.1)	Ref	0.07
	>0–239	576 (5.7)	66 (5.9)	1.03 (0.79, 1.35)	
	>239–1323	596 (5.9)	63 (5.6)	1.10 (0.82, 1.49)	
	>1323	576 (5.7)	73 (6.5)	1.35 (0.99, 1.84)	
Herbicide					
Alachlor	Never	7592 (44.9)	755 (41.4)	Ref	0.06
	>0–788	3114 (18.4)	332 (18.2)	1.00 (0.87, 1.15)	
	>788–2958	3140 (18.6)	371 (20.4)	1.11 (0.97, 1.27)	
	>2958	3056 (18.1)	364 (20)	1.11 (0.97, 1.27)	
Butylate <sup>b</sup>	Never	6940 (71.1)	726 (66.9)	Ref	0.02
	>0–455	943 (9.7)	119 (11)	1.12 (0.90, 1.38)	
	>455–1512	969 (9.9)	111 (10.2)	1.00 (0.80, 1.25)	
	>1512	908 (9.3)	130 (12.0)	1.26 (1.02, 1.55)	
Chlorimuron ethyl <sup>b</sup>	Never	6976 (68.0)	768 (67.0)	Ref	0.31
	>0–236	1124 (11.0)	133 (11.6)	1.11 (0.91, 1.35)	
	>236–662	1071 (10.4)	122 (10.6)	1.04 (0.84, 1.27)	
	>662	1084 (10.6)	124 (10.8)	1.09 (0.88, 1.33)	
Dicamba	Never	7653 (45.2)	750 (41.3)	Ref	0.72
	>0–551	3064 (18.1)	357 (19.6)	1.15 (1.00, 1.33)	
	>551–2170	3151 (18.6)	373 (20.5)	1.14 (0.99, 1.32)	
	>2170	3050 (18.0)	337 (18.5)	1.07 (0.92, 1.24)	
EPTC	Never	13280 (78.8)	1391 (76.9)	Ref	0.14
	>0–315	1209 (7.2)	129 (7.1)	0.97 (0.80, 1.18)	
	>315–1176	1216 (7.2)	152 (8.4)	1.14 (0.95, 1.36)	
	>1176	1143 (6.8)	137 (7.6)	1.09 (0.90, 1.31)	
Glyphosate	Never	4144 (23.1)	352 (18.3)	Ref	0.001
	>0–672	4559 (25.4)	541 (28.1)	1.42 (1.23, 1.64)	
	>672–2610	4724 (26.3)	491 (25.5)	1.24 (1.07, 1.44)	

	>2610	4548 (25.3)	539 (28.0)	1.45 (1.25, 1.68)	
Imazethapyr	Never	8889 (53.5)	936 (52.7)	Ref	0.89
	>0–338	2540 (15.3)	290 (16.3)	0.99 (0.85, 1.16)	
	>338–992	2664 (16)	274 (15.4)	0.90 (0.77, 1.05)	
	>992	2507 (15.1)	277 (15.6)	0.97 (0.83, 1.14)	
Metolachlor	Never	8866 (52.2)	922 (50.2)	Ref	0.13
	>0–720	2701 (15.9)	351 (19.1)	1.23 (1.07, 1.40)	
	>720–2604	2744 (16.2)	302 (16.4)	1.02 (0.89, 1.18)	
	>2604	2678 (15.8)	261 (14.2)	0.91 (0.78, 1.05)	
Paraquat <sup>b</sup>	Never	8765 (85.4)	949 (83.0)	Ref	0.03
	>0–275	500 (4.9)	64 (5.6)	1.18 (0.90, 1.56)	
	>275–1080	505 (4.9)	68 (5.9)	1.31 (1.00, 1.73)	
	>1080	492 (4.8)	63 (5.5)	1.33 (0.99, 1.79)	
Pendimethalin <sup>b</sup>	Never	6478 (63.2)	697 (60.7)	Ref	0.33
	>0–315	1276 (12.4)	146 (12.7)	1.03 (0.85, 1.25)	
	>315–1176	1242 (12.1)	170 (14.8)	1.30 (1.09, 1.56)	
	>1176	1259 (12.3)	135 (11.8)	1.04 (0.86, 1.27)	
Petroleum distillates <sup>b</sup>	Never	8018 (78.7)	844 (73.6)	Ref	0.01
	>0–502	731 (7.2)	96 (8.4)	1.22 (0.97, 1.53)	
	>502–2438	726 (7.1)	107 (9.3)	1.39 (1.12, 1.73)	
	>2438	708 (7.0)	99 (8.6)	1.29 (1.03, 1.62)	
Trifluralin	Never	7267 (45.1)	697 (40.4)	Ref	0.05
	>0–1020	2948 (18.3)	312 (18.1)	1.04 (0.89, 1.21)	
	>1020–3875	3019 (18.7)	360 (20.8)	1.14 (0.98, 1.32)	
	>3875	2878 (17.9)	358 (20.7)	1.15 (0.98, 1.34)	
2,4-D	Never	3981 (22.3)	346 (18.1)	Ref	0.01
	>0–1302	4620 (25.9)	489 (25.6)	1.14 (0.98, 1.33)	
	>1302–5208	4836 (27.1)	512 (26.8)	1.08 (0.93, 1.26)	
	>5208	4431 (24.8)	563 (29.5)	1.21 (1.04, 1.41)	
2,4,5-T <sup>b</sup>	Never	7960 (82.2)	772 (71.7)	Ref	0.01
	>0–280	562 (5.8)	105 (9.8)	1.64 (1.30, 2.06)	
	>280–971	583 (6.0)	108 (10.0)	1.66 (1.32, 2.09)	
	>971	573 (5.9)	91 (8.5)	1.40 (1.10, 1.80)	
2,4,5-TP <sup>b</sup>	Never	9239 (95.3)	998 (92.5)	Ref	0.22
	>0–315	158 (1.6)	25 (2.3)	1.20 (0.77, 1.86)	
	>315–1250	148 (1.5)	32 (3.0)	1.61 (1.08, 2.41)	
	>1250	148 (1.5)	24 (2.2)	1.19 (0.76, 1.86)	
Atrazine	Never	4831 (26.8)	447 (23.3)	Ref	0.26
	>0–1054	4369 (24.3)	484 (25.2)	1.14 (0.99, 1.31)	
	>1054–4340	4497 (25.0)	491 (25.6)	1.08 (0.93, 1.25)	
	>4340	4299 (23.9)	495 (25.8)	1.10 (0.96, 1.28)	
Cyanazine	Never	9433 (55.5)	952 (52.0)	Ref	0.15
	>0–539	2496 (14.7)	299 (16.3)	1.11 (0.96, 1.28)	
	>539–2200	2581 (15.2)	283 (15.4)	1.00 (0.86, 1.16)	
	>2200	2475 (14.6)	298 (16.3)	1.10 (0.95, 1.27)	
Metribuzin <sup>b</sup>	Never	5525 (58.3)	560 (53.3)	Ref	0.01
	>0–315	1317 (13.9)	145 (13.8)	0.99 (0.80, 1.22)	
	>315–1000	1353 (14.3)	162 (15.4)	1.08 (0.89, 1.33)	
	>1000	1277 (13.5)	183 (17.4)	1.26 (1.04, 1.54)	

Abbreviation: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; 2,4,5-T,P, 2-(2,4,5-trichlorophenoxy) propionic acid; CI, Confidence Intervals; CCl<sub>4</sub>/CS<sub>2</sub>, Carbon tetrachloride/Carbon disulfide 80/20

mix; DDT, Dichlorodiphenyltrichloroethane; EPTC, S-Ethyl dipropylthiocarbamate; OI, Olfactory Impairment; OR, Odds Ratio

Odds ratios are adjusted for age, sex, state of residence, education, smoking status, ever performed following tasks at least once each year (repair engines, replace asbestos brake linings, handle stored grain, work in swine confinement areas, weld and paint), and correlated pesticides (correlated ever-use of pesticides with Spearman correlation  $\geq 0.40$ )

<sup>a</sup>Exposure categories: Never-use and categorized into tertiles among users

<sup>b</sup>Frequency and duration of pesticide was asked only in the take-home questionnaire

Supplementary table 5: Lifetime days (unweighted) of use at enrollment in relation to self-reported olfactory impairment in the Agricultural Health Study

Pesticides	Days	No OI, n (%)	OI, n (%)	OR (95% CI)	P
Aldrin	Never use	8080 (83.9)	849 (75.7)	Ref	0.17
	Tertile 1	752 (7.8)	122 (10.9)	1.06 (0.84, 1.32)	
	Tertile 2	460 (4.8)	78 (7.0)	1.06 (0.80, 1.40)	
	Tertile 3	344 (3.6)	72 (6.4)	1.24 (0.92, 1.67)	
Chlordane	Never use	8080 (82.0)	857 (73.1)	Ref	0.003
	Tertile 1	480 (4.9)	83 (7.1)	1.43 (1.11, 1.84)	
	Tertile 2	726 (7.4)	119 (10.2)	1.23 (0.99, 1.52)	
	Tertile 3	568 (5.8)	113 (9.6)	1.40 (1.12, 1.75)	
Dieldrin	Never use	9363 (96.7)	1074 (94.5)		0.96
	Tertile 1	80 (0.8)	13 (1.1)	0.91 (0.50, 1.67)	
	Tertile 2	133 (1.4)	32 (2.8)	1.26 (0.84, 1.90)	
	Tertile 3	106 (1.1)	17 (1.5)	0.89 (0.52, 1.50)	
DDT	Never use	7873 (81.2)	794 (69.4)	Ref	0.04
	Tertile 1	848 (8.8)	159 (13.9)	1.33 (1.08, 1.63)	
	Tertile 2	380 (3.9)	72 (6.3)	1.31 (0.99, 1.74)	
	Tertile 3	589 (6.1)	119 (10.4)	1.34 (1.06, 1.69)	
Heptachlor	Never use	8535 (88.1)	938 (82.4)	Ref	0.10
	Tertile 1	590 (6.1)	96 (8.4)	1.06 (0.83, 1.36)	
	Tertile 2	325 (3.4)	50 (4.4)	0.96 (0.70, 1.33)	
	Tertile 3	241 (2.5)	54 (4.7)	1.37 (0.99, 1.89)	
Toxaphene	Never use	9303 (90.1)	1050 (85.7)	Ref	0.05
	Tertile 1	538 (5.2)	88 (7.2)	1.25 (0.99, 1.59)	
	Tertile 2	234 (2.3)	43 (3.5)	1.35 (0.96, 1.89)	
	Tertile 3	251 (2.4)	44 (3.6)	1.32 (0.95, 1.85)	
Lindane	Never use	8777 (85.5)	957 (78.4)	Ref	<.0001
	Tertile 1	696 (6.8)	118 (9.7)	1.38 (1.12, 1.71)	
	Tertile 2	330 (3.2)	46 (3.8)	1.14 (0.83, 1.58)	
	Tertile 3	460 (4.5)	99 (8.1)	1.78 (1.41, 2.25)	
Aldicarb	Never use	9177 (93.3)	1099 (94.3)	Ref	0.02
	Tertile 1	217 (2.2)	23 (2.0)	0.94 (0.60, 1.48)	
	Tertile 2	267 (2.7)	35 (3.0)	1.21 (0.82, 1.78)	
	Tertile 3	179 (1.8)	9 (0.8)	0.43 (0.21, 0.86)	
Carbaryl	Never use	5720 (58.8)	605 (52.4)	Ref	0.33
	Tertile 1	1731 (17.8)	253 (21.9)	1.26 (1.07, 1.48)	
	Tertile 2	998 (10.3)	130 (11.3)	1.13 (0.91, 1.41)	
	Tertile 3	1272 (13.1)	167 (14.5)	1.18 (0.95, 1.48)	
Carbofuran	Never use	12143 (71.4)	1278 (65.9)	Ref	0.07
	Tertile 1	1976 (11.6)	272 (14.0)	1.18 (1.02, 1.35)	
	Tertile 2	1279 (7.5)	182 (9.4)	1.21 (1.02, 1.43)	
	Tertile 3	1600 (9.4)	206 (10.6)	1.12 (0.95, 1.31)	
Chlorpyrifos	Never use	10324 (57.1)	1094 (53.6)	Ref	0.06
	Tertile 1	2614 (14.4)	338 (16.6)	1.22 (1.07, 1.39)	
	Tertile 2	2678 (14.8)	303 (14.8)	1.05 (0.92, 1.21)	
	Tertile 3	2475 (13.7)	307 (15.0)	1.17 (1.02, 1.34)	
Coumaphos	Never use	15237 (90.6)	1694 (88.8)	Ref	0.67
	Tertile 1	671 (4.0)	100 (5.2)	1.25 (1.00, 1.55)	
	Tertile 2	447 (2.7)	65 (3.4)	1.24 (0.95, 1.62)	
	Tertile 3	468 (2.8)	48 (2.5)	0.88 (0.65, 1.19)	

Diazinon	Never use	7891 (79.4)	866 (72.9)	Ref	0.00
	Tertile 1	1026 (10.3)	153 (12.9)	1.29 (1.07, 1.56)	
	Tertile 2	445 (4.5)	77 (6.5)	1.39 (1.07, 1.80)	
	Tertile 3	574 (5.8)	92 (7.7)	1.45 (1.14, 1.86)	
DDVP	Never use	14963 (87.8)	1631 (84.3)	Ref	0.03
	Tertile 1	816 (4.8)	108 (5.6)	1.12 (0.91, 1.39)	
	Tertile 2	679 (4.0)	106 (5.5)	1.32 (1.06, 1.63)	
	Tertile 3	581 (3.4)	89 (4.6)	1.28 (1.01, 1.61)	
Fonofos	Never use	13161 (76.8)	1462 (75.0)	Ref	0.37
	Tertile 1	1638 (9.6)	208 (10.7)	1.06 (0.90, 1.24)	
	Tertile 2	1137 (6.6)	139 (7.1)	0.99 (0.82, 1.20)	
	Tertile 3	1200 (7.0)	141 (7.2)	0.92 (0.76, 1.11)	
Malathion	Never use	3562 (34.8)	345 (28.3)	Ref	0.01
	Tertile 1	2732 (26.7)	331 (27.2)	1.18 (1.01, 1.39)	
	Tertile 2	2165 (21.1)	284 (23.3)	1.25 (1.05, 1.48)	
	Tertile 3	1784 (17.4)	258 (21.2)	1.34 (1.12, 1.60)	
Parathion	Never use	9549 (93.1)	1099 (90.5)	Ref	0.49
	Tertile 1	309 (3.0)	59 (4.9)	1.53 (1.14, 2.05)	
	Tertile 2	173 (1.7)	27 (2.2)	1.32 (0.86, 2.00)	
	Tertile 3	227 (2.2)	29 (2.4)	1.09 (0.73, 1.62)	
Phorate	Never use	6682 (67.8)	741 (63.6)	Ref	0.90
	Tertile 1	1334 (13.5)	180 (15.4)	1.08 (0.90, 1.29)	
	Tertile 2	869 (8.8)	126 (10.8)	1.16 (0.94, 1.43)	
	Tertile 3	974 (9.9)	119 (10.2)	0.95 (0.77, 1.17)	
Terbufos	Never use	10144 (59.3)	1100 (56.4)	Ref	0.09
	Tertile 1	2519 (14.7)	295 (15.1)	1.04 (0.91, 1.2)	
	Tertile 2	2418 (14.1)	290 (14.9)	1.07 (0.93, 1.23)	
	Tertile 3	2034 (11.9)	265 (13.6)	1.14 (0.98, 1.32)	
Permethrin (crops)	Never use	14691 (86.7)	1626 (84.9)	Ref	0.02
	Tertile 1	1199 (7.1)	153 (8.0)	1.17 (0.98, 1.39)	
	Tertile 2	410 (2.4)	52 (2.7)	1.24 (0.92, 1.67)	
	Tertile 3	642 (3.8)	84 (4.4)	1.3 (1.02, 1.65)	
Permethrin (animals)	Never use	14569 (84.8)	1611 (82.7)	Ref	0.28
	Tertile 1	1078 (6.3)	157 (8.1)	1.35 (1.13, 1.62)	
	Tertile 2	685 (4.0)	79 (4.1)	1.08 (0.85, 1.38)	
	Tertile 3	844 (4.9)	101 (5.2)	1.13 (0.91, 1.40)	
CCl <sub>4</sub> /CS <sub>2</sub>	Never use	9947 (96.2)	1146 (93.2)	Ref	0.13
	Tertile 1	188 (1.8)	39 (3.2)	1.40 (0.98, 2.00)	
	Tertile 2	97 (0.9)	21 (1.7)	1.36 (0.84, 2.21)	
	Tertile 3	111 (1.1)	23 (1.9)	1.34 (0.84, 2.12)	
Aluminum Phosphide	Never use	9963 (96.2)	1181 (95.8)	Ref	0.81
	Tertile 1	211 (2.0)	32 (2.6)	1.22 (0.83, 1.78)	
	Tertile 2	108 (1.0)	11 (0.9)	0.88 (0.47, 1.65)	
	Tertile 3	70 (0.7)	9 (0.7)	1.10 (0.54, 2.22)	
Ethylene Dibromide	Never use	9937 (96.0)	1182 (95.6)	Ref	0.90
	Tertile 1	151 (1.5)	18 (1.5)	1.06 (0.64, 1.75)	
	Tertile 2	156 (1.5)	28 (2.3)	1.55 (1.01, 2.36)	
	Tertile 3	104 (1.0)	9 (0.7)	0.76 (0.38, 1.52)	
Methyl Bromide	Never use	14752 (86.5)	1673 (86.9)	Ref	0.17
	Tertile 1	895 (5.2)	89 (4.6)	0.95 (0.74, 1.21)	
	Tertile 2	676 (4.0)	66 (3.4)	0.87 (0.65, 1.17)	

	Tertile 3	732 (4.3)	98 (5.1)	1.18 (0.92, 1.53)	
Benomyl	Never use	8920 (93.5)	1041 (92.3)	Ref	0.20
	Tertile 1	302 (3.2)	42 (3.7)	1.32 (0.93, 1.89)	
	Tertile 2	116 (1.2)	16 (1.4)	1.34 (0.76, 2.35)	
	Tertile 3	199 (2.1)	29 (2.6)	1.41 (0.90, 2.23)	
Captan	Never use	14939 (89.3)	1649 (86.8)	Ref	0.04
	Tertile 1	1080 (6.5)	150 (7.9)	1.24 (1.03, 1.48)	
	Tertile 2	137 (0.8)	17 (0.9)	1.08 (0.65, 1.79)	
	Tertile 3	566 (3.4)	83 (4.4)	1.31 (1.03, 1.67)	
Chlorothalonil	Never use	15927 (93.6)	1791 (93.4)	Ref	0.92
	Tertile 1	365 (2.1)	50 (2.6)	1.27 (0.93, 1.74)	
	Tertile 2	339 (2.0)	39 (2.0)	1.13 (0.79, 1.63)	
	Tertile 3	378 (2.2)	38 (2.0)	1.03 (0.71, 1.49)	
Maneb/Mancozeb	Never use	9138 (93.1)	1089 (93.2)	Ref	0.89
	Tertile 1	310 (3.2)	27 (2.3)	0.73 (0.48, 1.11)	
	Tertile 2	191 (1.9)	33 (2.8)	1.41 (0.94, 2.12)	
	Tertile 3	179 (1.8)	20 (1.7)	0.89 (0.54, 1.45)	
Metalaxy1	Never use	8441 (82.8)	996 (82.1)	Ref	0.05
	Tertile 1	630 (6.2)	79 (6.5)	1.08 (0.84, 1.39)	
	Tertile 2	683 (6.7)	79 (6.5)	1.12 (0.85, 1.47)	
	Tertile 3	442 (4.3)	59 (4.9)	1.40 (1.01, 1.94)	
Alachlor	Never use	7642 (44.9)	795 (41.0)	Ref	0.01
	Tertile 1	4219 (24.8)	484 (25.0)	1.02 (0.91, 1.16)	
	Tertile 2	2097 (12.3)	249 (12.8)	1.05 (0.90, 1.23)	
	Tertile 3	3051 (17.9)	411 (21.2)	1.18 (1.04, 1.35)	
Butylate	Never use	6975 (71.1)	790 (67.8)	Ref	0.10
	Tertile 1	982 (10.0)	132 (11.3)	1.08 (0.88, 1.33)	
	Tertile 2	1085 (11.1)	125 (10.7)	0.94 (0.77, 1.16)	
	Tertile 3	773 (7.9)	119 (10.2)	1.22 (0.98, 1.51)	
Chlorimuron Ethyl	Never use	7021 (68.0)	828 (67.3)	Ref	0.43
	Tertile 1	2147 (20.8)	265 (21.5)	1.07 (0.92, 1.24)	
	Tertile 2	117 (1.1)	11 (0.9)	0.73 (0.39, 1.36)	
	Tertile 3	1033 (10.0)	126 (10.2)	1.10 (0.90, 1.35)	
Dicamba	Never use	7708 (45.2)	794 (41.0)	Ref	0.43
	Tertile 1	3972 (23.3)	501 (25.9)	1.16 (1.02, 1.33)	
	Tertile 2	2796 (16.4)	322 (16.6)	1.07 (0.92, 1.24)	
	Tertile 3	2560 (15.0)	318 (16.4)	1.13 (0.97, 1.31)	
EPTC	Never use	13365 (78.9)	1488 (77.3)	Ref	0.13
	Tertile 1	1662 (9.8)	191 (9.9)	0.97 (0.82, 1.14)	
	Tertile 2	822 (4.9)	97 (5.0)	1.01 (0.81, 1.26)	
	Tertile 3	1096 (6.5)	148 (7.7)	1.15 (0.96, 1.38)	
Glyphosate	Never use	4166 (23.0)	381 (18.6)	Ref	0.00
	Tertile 1	5728 (31.6)	680 (33.2)	1.31 (1.15, 1.50)	
	Tertile 2	4176 (23.1)	472 (23.1)	1.28 (1.11, 1.48)	
	Tertile 3	4031 (22.3)	513 (25.1)	1.44 (1.24, 1.66)	
Imazethapyr	Never use	8947 (53.6)	1001 (52.9)	Ref	0.27
	Tertile 1	3400 (20.4)	416 (22.0)	1.00 (0.87, 1.14)	
	Tertile 2	2510 (15.0)	268 (14.2)	0.88 (0.75, 1.03)	
	Tertile 3	1841 (11.0)	207 (10.9)	0.94 (0.79, 1.12)	
Metolachlor	Never use	8929 (52.2)	989 (50.6)	Ref	0.20
	Tertile 1	2730 (16.0)	376 (19.3)	1.20 (1.06, 1.37)	

	Tertile 2	2908 (17.0)	305 (15.6)	0.92 (0.80, 1.05)		
	Tertile 3	2530 (14.8)	283 (14.5)	0.96 (0.84, 1.11)		
Paraquat	Never use	8817 (85.4)	1022 (83.2)	Ref	0.05	
	Tertile 1	838 (8.1)	121 (9.9)	1.25 (1.02, 1.54)		
	Tertile 2	274 (2.7)	29 (2.4)	0.99 (0.66, 1.48)		
	Tertile 3	394 (3.8)	56 (4.6)	1.39 (1.01, 1.90)		
Pendimethalin	Never use	6521 (63.2)	755 (61.3)	Ref	0.62	
	Tertile 1	1698 (16.5)	229 (18.6)	1.13 (0.97, 1.33)		
	Tertile 2	967 (9.4)	122 (9.9)	1.14 (0.93, 1.40)		
	Tertile 3	1132 (11.0)	126 (10.2)	1.02 (0.83, 1.25)		
Petroleum	Never use	8058 (78.7)	911 (74.1)	Ref	0.04	
	Tertile 1	732 (7.1)	102 (8.3)	1.21 (0.97, 1.51)		
	Tertile 2	812 (7.9)	120 (9.8)	1.30 (1.06, 1.60)		
	Tertile 3	642 (6.3)	96 (7.8)	1.27 (1.01, 1.60)		
Trifluralin	Never use	7301 (45.0)	742 (40.5)	Ref	0.16	
	Tertile 1	3029 (18.7)	343 (18.7)	1.05 (0.90, 1.21)		
	Tertile 2	3540 (21.8)	440 (24.0)	1.09 (0.95, 1.27)		
	Tertile 3	2339 (14.4)	309 (16.8)	1.14 (0.97, 1.34)		
2,4-D	Never use	4004 (22.3)	364 (17.9)	Ref	0.19	
	Tertile 1	5538 (30.8)	606 (29.8)	1.12 (0.97, 1.29)		
	Tertile 2	4234 (23.5)	503 (24.8)	1.14 (0.98, 1.33)		
	Tertile 3	4217 (23.4)	558 (27.5)	1.16 (1.00, 1.35)		
2,4,5 T	Never use	7999 (82.2)	828 (71.6)	Ref	0.05	
	Tertile 1	980 (10.1)	194 (16.8)	1.62 (1.35, 1.94)		
	Tertile 2	320 (3.3)	63 (5.4)	1.60 (1.20, 2.15)		
	Tertile 3	435 (4.5)	71 (6.1)	1.32 (1.01, 1.74)		
2,4,5 T P	Never use	9291 (95.3)	1071 (92.5)	Ref	0.24	
	Tertile 1	229 (2.3)	43 (3.7)	1.34 (0.94, 1.89)		
	Tertile 2	88 (0.9)	19 (1.6)	1.48 (0.89, 2.48)		
	Tertile 3	138 (1.4)	25 (2.2)	1.24 (0.79, 1.93)		
Atrazine	Never use	4863 (26.8)	473 (23.2)	Ref	0.24	
	Tertile 1	4413 (24.4)	503 (24.7)	1.12 (0.97, 1.28)		
	Tertile 2	4930 (27.2)	567 (27.8)	1.05 (0.92, 1.21)		
	Tertile 3	3913 (21.6)	495 (24.3)	1.13 (0.98, 1.31)		
Cyanazine	Never use	9498 (55.6)	1008 (51.7)	Ref	0.37	
	Tertile 1	3076 (18.0)	381 (19.5)	1.07 (0.94, 1.22)		
	Tertile 2	2434 (14.2)	297 (15.2)	1.06 (0.92, 1.23)		
	Tertile 3	2090 (12.2)	263 (13.5)	1.08 (0.93, 1.26)		
Metribuzin	Never use	5550 (58.3)	605 (53.6)	Ref	0.10	
	Tertile 1	1916 (20.1)	248 (22.0)	1.08 (0.91, 1.29)		
	Tertile 2	1052 (11.0)	131 (11.6)	1.05 (0.85, 1.31)		
	Tertile 3	1003 (10.5)	144 (12.8)	1.21 (0.98, 1.50)		

Abbreviation: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; CI, Confidence Intervals; EPTC, S-Ethyl dipropylthiocarbamate; OI, Olfactory Impairment; OR, Odds Ratio

Odds ratios are adjusted for age, sex, state of residence, education, smoking status, ever performed following tasks at least once each year (repair engines, replace asbestos brake linings, handle stored grain, work in swine confinement areas, weld and paint), and correlated pesticides (correlated ever-use of pesticides with Spearman correlation  $\geq 0.40$ )

<sup>a</sup>Exposure categories: Never use and categorized into tertiles among users

**Supplementary table 6: Average days per year of use at enrollment in relation to self-reported olfactory impairment in the Agricultural Health Study**

Pesticide	Days	No OI	OR (95% CI)	P
Aldrin	0 d	849 (75.7)	Ref	0.32
	<5 d	141 (12.6)	1.09 (0.87, 1.35)	
	5-9 d	94 (8.4)	1.07 (0.83, 1.38)	
	> 10 d	38 (3.4)	1.21 (0.83, 1.78)	
Chlordane	0 d	857 (73.0)	Ref	0.01
	<5 d	246 (21)	1.37 (1.16, 1.61)	
	5-9 d	49 (4.2)	1.14 (0.82, 1.56)	
	> 10 d	22 (1.9)	1.62 (1.00, 2.62)	
DDT	0 d	794 (69.3)	Ref	0.01
	<5 d	191 (16.7)	1.33 (1.10, 1.62)	
	5-9 d	76 (6.6)	1.16 (0.89, 1.53)	
	10-19 d	42 (3.7)	1.28 (0.90, 1.83)	
	20-39 d	27 (2.4)	2.09 (1.34, 3.27)	
Heptachlor	>40 d	15 (1.3)	1.35 (0.76, 2.41)	
	0 d	938 (82.3)	Ref	0.16
	<5 d	113 (9.9)	1.13 (0.90, 1.42)	
	5-9 d	57 (5.0)	0.92 (0.68, 1.25)	
Toxaphene	> 10 d	32 (2.8)	1.54 (1.02, 2.32)	
	0 d	1050 (85.6)	Ref	0.01
	<5 d	109 (8.9)	1.34 (1.08, 1.67)	
	5-9 d	37 (3.0)	1.04 (0.73, 1.49)	
	10-19 d	16 (1.3)	1.19 (0.69, 2.05)	
Lindane	>20 d	14 (1.1)	2.31 (1.26, 4.25)	
	0 d	957 (78.4)	Ref	<.0001
	<5 d	163 (13.3)	1.40 (1.17, 1.68)	
	5-9 d	56 (4.6)	1.33 (0.99, 1.78)	
	10-19 d	27 (2.2)	1.55 (1.02, 2.36)	
Aldicarb	>20 d	18 (1.5)	3.07 (1.76, 5.35)	
	0 d	1099 (94.3)	Ref	0.10
	<5 d	31 (2.7)	1.02 (0.68, 1.51)	
	5-9 d	25 (2.1)	1.12 (0.72, 1.74)	
Carbaryl	>10 d	11 (0.9)	0.51 (0.27, 0.96)	
	0 d	605 (52.3)	Ref	0.06
	<5 d	345 (29.8)	1.24 (1.07, 1.44)	
	5-9 d	112 (9.7)	1.08 (0.85, 1.36)	
	10-19 d	62 (5.4)	1.30 (0.96, 1.77)	
Carbofuran	>20 d	32 (2.8)	1.43 (0.95, 2.15)	
	0 d	1278 (65.9)	Ref	0.03
	<5 d	314 (16.2)	1.14 (0.99, 1.30)	
	5-9 d	216 (11.1)	1.22 (1.04, 1.43)	
	10-19 d	102 (5.3)	1.11 (0.89, 1.38)	
Chlorpyrifos	>20 d	29 (1.5)	1.26 (0.84, 1.87)	
	0 d	1094 (53.5)	Ref	0.27
	<5 d	469 (23.0)	1.19 (1.06, 1.33)	
	5-9 d	294 (14.4)	1.14 (0.99, 1.31)	
	10-19 d	141 (6.9)	1.03 (0.86, 1.24)	
Coumaphos	>20 d	45 (2.2)	1.15 (0.84, 1.58)	
	0 d	1694 (88.8)	Ref	0.97

	<5 d	147 (7.7)	1.23 (1.02, 1.47)		
	5-9 d	42 (2.2)	1.12 (0.81, 1.55)		
	10-19 d	10 (0.5)	0.59 (0.31, 1.13)		
	>20 d	14 (0.7)	1.06 (0.6, 1.86)		
Diazinon	0 d	866 (72.9)	Ref	0.0008	
	<5 d	193 (16.2)	1.29 (1.09, 1.54)		
	5-9 d	83 (7.0)	1.39 (1.08, 1.79)		
	10-19 d	32 (2.7)	1.54 (1.04, 2.28)		
	>20 d	14 (1.2)	1.64 (0.91, 2.96)		
Dicholrvos	0 d	1631 (84.3)	Ref	0.03	
	<5 d	119 (6.2)	1.12 (0.92, 1.38)		
	5-9 d	61 (3.2)	1.33 (1.00, 1.76)		
	10-19 d	43 (2.2)	1.28 (0.92, 1.77)		
	20-39 d	27 (1.4)	1.13 (0.75, 1.70)		
	40-59 d	22 (1.1)	1.56 (0.98, 2.47)		
	>60 d	31 (1.6)	1.29 (0.88, 1.90)		
Fonofos	0 d	1462 (75.0)	Ref	0.71	
	<5 d	228 (11.7)	1.09 (0.94, 1.27)		
	5-9 d	148 (7.6)	0.87 (0.72, 1.04)		
	10-19 d	94 (4.8)	1.01 (0.81, 1.27)		
	>20 d	18 (0.9)	1.03 (0.63, 1.70)		
Malathion	0 d	345 (28.3)	Ref	0.01	
	<5 d	586 (48)	1.21 (1.05, 1.40)		
	5-9 d	178 (14.6)	1.28 (1.05, 1.56)		
	10-19 d	74 (6.1)	1.34 (1.02, 1.76)		
	20-39 d	23 (1.9)	1.29 (0.82, 2.03)		
	>40 d	15 (1.2)	1.76 (0.99, 3.13)		
Parathion	0 d	1099 (90.5)	Ref	0.34	
	<5 d	66 (5.4)	1.41 (1.07, 1.87)		
	5-9 d	27 (2.2)	1.39 (0.91, 2.12)		
	10-19 d	12 (1.0)	1.07 (0.58, 1.97)		
	>20 d	10 (0.8)	1.09 (0.56, 2.14)		
Phorate	0 d	741 (63.5)	Ref	0.47	
	<5 d	222 (19.0)	1.11 (0.94, 1.32)		
	5-9 d	149 (12.8)	1.07 (0.88, 1.30)		
	>10 d	55 (4.7)	0.85 (0.64, 1.15)		
Terbufos	0 d	1100 (56.3)	Ref	0.08	
	<5 d	337 (17.3)	1.06 (0.93, 1.21)		
	5-9 d	280 (14.3)	1.04 (0.90, 1.20)		
	10-19 d	188 (9.6)	1.17 (0.99, 1.38)		
	>20 d	48 (2.5)	1.15 (0.85, 1.57)		
Permethrin (crops)	0 d	1626 (84.8)	Ref	0.01	
	<5 d	168 (8.8)	1.15 (0.97, 1.36)		
	5-9 d	60 (3.1)	1.32 (1.00, 1.74)		
	10-19 d	37 (1.9)	1.28 (0.90, 1.82)		
	>20 d	26 (1.4)	1.46 (0.96, 2.22)		
Permethrin (poultry)	0 d	1611 (82.7)	Ref	0.28	
	<5 d	196 (10.1)	1.24 (1.05, 1.46)		
	5-9 d	70 (3.6)	1.17 (0.91, 1.52)		
	10-19 d	43 (2.2)	1.27 (0.92, 1.76)		
	20-39 d	14 (0.7)	1.01 (0.58, 1.77)		

	>40 d	15 (0.8)	1.10 (0.64, 1.89)	
CCl <sub>4</sub> /CS <sub>2</sub>	0 d	1146 (93.1)	Ref	0.02
	1 d	35 (2.8)	1.4 (0.96, 2.04)	
	>2 d	50 (4.1)	1.38 (1.00, 1.9)	
Aluminum Phosphide	0 d	1181 (95.8)	Ref	0.55
	1 d	29 (2.4)	1.10 (0.74, 1.63)	
	>2 d	23 (1.9)	1.12 (0.72, 1.74)	
Ethylene Dibromide	0 d	1182 (95.6)	Ref	0.35
	1 d	24 (1.9)	1.13 (0.73, 1.75)	
	>2 d	31 (2.5)	1.19 (0.80, 1.77)	
Methyl Bromide	0 d	1673 (86.8)	Ref	0.87
	1 d	118 (6.1)	1.03 (0.83, 1.30)	
	2-5 d	107 (5.6)	0.98 (0.77, 1.24)	
	6-10 d	14 (0.7)	0.74 (0.42, 1.30)	
	>11 d	15 (0.8)	1.15 (0.66, 2.00)	
Benomyl	0 d	1041 (92.3)	Ref	0.27
	1 d	22 (2.0)	1.6 (1.00, 2.56)	
	2-5 d	24 (2.1)	0.98 (0.62, 1.57)	
	5-9 d	25 (2.2)	1.78 (1.1, 2.87)	
	>10 d	16 (1.4)	1.13 (0.64, 2.00)	
Captan	0 d	1649 (86.2)	Ref	0.01
	1 d	169 (8.8)	1.23 (1.04, 1.46)	
	2-5 d	32 (1.7)	1.14 (0.78, 1.66)	
	6-10 d	34 (1.8)	1.49 (1.03, 2.17)	
	11-20 d	18 (0.9)	1.38 (0.83, 2.28)	
	>20 d	12 (0.6)	1.63 (0.87, 3.05)	
Chlorothalonil	0 d	1791 (93.3)	Ref	0.21
	1 d	21 (1.1)	1.17 (0.73, 1.86)	
	2-5 d	41 (2.1)	1.17 (0.83, 1.66)	
	6-10 d	29 (1.5)	0.96 (0.64, 1.45)	
	>11 d	38 (2.0)	1.31 (0.91, 1.90)	
Maneb/Mancozeb	0 d	1089 (93.1)	Ref	0.99
	1 d	13 (1.1)	0.97 (0.54, 1.74)	
	2-5 d	23 (2.0)	0.72 (0.45, 1.14)	
	5-9 d	26 (2.2)	1.37 (0.87, 2.16)	
	>10 d	19 (1.6)	0.92 (0.55, 1.52)	
Metalaxy1	0 d	996 (81.9)	Ref	0.02
	1 d	64 (5.3)	1.12 (0.85, 1.47)	
	2-5 d	96 (7.9)	1.09 (0.85, 1.40)	
	5-9 d	34 (2.8)	1.13 (0.76, 1.66)	
	>10 d	26 (2.1)	1.74 (1.11, 2.73)	
Alachlor	0 d	795 (41.0)	Ref	0.61
	<5 d	458 (23.6)	1.11 (0.98, 1.25)	
	5-9 d	368 (19.0)	1.00 (0.87, 1.14)	
	10-19 d	251 (12.9)	1.23 (1.06, 1.44)	
	20-39 d	55 (2.8)	0.89 (0.67, 1.19)	
	>40 d	12 (0.6)	1.01 (0.55, 1.85)	
Butylate	0 d	790 (67.8)	Ref	0.19
	<5 d	148 (12.7)	1.03 (0.85, 1.25)	
	5-9 d	145 (12.4)	1.00 (0.82, 1.22)	

	10-19 d	71 (6.1)	1.37 (1.05, 1.80)	
	>20 d	12 (1.0)	0.97 (0.53, 1.79)	
Chlorimuron Ethyl	0 d	828 (67.3)	Ref	0.31
	<5 d	275 (22.3)	1.05 (0.90, 1.21)	
	5-9 d	94 (7.6)	1.07 (0.85, 1.35)	
	>10 d	34 (2.8)	1.16 (0.80, 1.68)	
Dicamba	0 d	794 (41.0)	Ref	0.47
	<5 d	656 (33.8)	1.18 (1.04, 1.33)	
	5-9 d	324 (16.7)	1.04 (0.90, 1.21)	
	10-19 d	123 (6.3)	1.06 (0.86, 1.31)	
EPTC	>20 d	41 (2.1)	1.27 (0.90, 1.78)	
	0 d	1488 (77.2)	Ref	0.35
	<5 d	215 (11.2)	0.96 (0.83, 1.13)	
	5-9 d	145 (7.5)	1.17 (0.97, 1.41)	
	10-19 d	59 (3.1)	1.04 (0.79, 1.38)	
Glyphosate	>20 d	20 (1.0)	1.08 (0.67, 1.72)	
	0 d	381 (18.6)	Ref	0.003
	<5 d	756 (36.9)	1.29 (1.13, 1.47)	
	5-9 d	457 (22.3)	1.28 (1.11, 1.48)	
	10-19 d	330 (16.1)	1.54 (1.31, 1.81)	
	20-39 d	100 (4.9)	1.43 (1.13, 1.82)	
	40-59 d	13 (0.6)	1.18 (0.66, 2.11)	
Imazethapyr	>60 d	11 (0.5)	1.67 (0.87, 3.19)	
	0 d	1001 (52.9)	Ref	0.61
	<5 d	456 (24.1)	0.99 (0.86, 1.13)	
	5-9 d	292 (15.4)	0.86 (0.74, 1.00)	
	10-19 d	119 (6.3)	1.05 (0.85, 1.3)	
Metolachlor	>20 d	26 (1.4)	0.94 (0.62, 1.42)	
	0 d	989 (50.6)	Ref	0.21
	<5 d	424 (21.7)	1.19 (1.05, 1.35)	
	5-9 d	319 (16.3)	0.94 (0.82, 1.08)	
	10-19 d	168 (8.6)	0.89 (0.75, 1.06)	
Paraquat	>20 d	55 (2.8)	1.01 (0.75, 1.35)	
	0 d	1022 (83.2)	Ref	0.002
	<5 d	135 (11.0)	1.19 (0.97, 1.45)	
	5-9 d	34 (2.8)	1.02 (0.70, 1.48)	
	10-19 d	23 (1.9)	1.72 (1.08, 2.75)	
Pendimethalin	>20 d	14 (1.1)	2.06 (1.13, 3.75)	
	0 d	755 (61.3)	Ref	0.18
	<5 d	251 (20.4)	1.07 (0.92, 1.25)	
	5-9 d	156 (12.7)	1.13 (0.94, 1.37)	
	10-19 d	54 (4.4)	1.13 (0.84, 1.53)	
Petroleum	>20 d	16 (1.3)	1.16 (0.68, 1.98)	
	0 d	911 (74.1)	Ref	0.04
	<5 d	160 (13.0)	1.28 (1.07, 1.54)	
	5-9 d	81 (6.6)	1.15 (0.90, 1.47)	
	10-19 d	41 (3.3)	1.35 (0.96, 1.89)	
Trifluralin	20-39 d	16 (1.3)	1.24 (0.73, 2.11)	
	>40 d	20 (1.6)	1.36 (0.84, 2.20)	
	0 d	742 (40.4)	Ref	0.15
	<5 d	412 (22.4)	1.05 (0.91, 1.21)	

	5-9 d	422 (23.0)	1.11 (0.96, 1.29)		
	10-19 d	198 (10.8)	1.06 (0.88, 1.27)		
	>20 d	63 (3.4)	1.24 (0.93, 1.65)		
2,4-D	0 d	364 (17.9)	Ref	0.67	
	<5 d	717 (35.2)	1.17 (1.02, 1.34)		
	5-9 d	487 (23.9)	1.05 (0.91, 1.23)		
	10-19 d	325 (16.0)	1.21 (1.02, 1.43)		
	20-39 d	112 (5.5)	1.12 (0.89, 1.41)		
	40-59 d	21 (1.0)	1.16 (0.72, 1.86)		
	>60 d	10 (0.5)	1.00 (0.51, 1.95)		
2,4,5 T	0 d	828 (71.6)	Ref	0.0002	
	<5 d	238 (20.6)	1.56 (1.32, 1.85)		
	5-9 d	60 (5.2)	1.45 (1.08, 1.94)		
	>10 d	30 (2.6)	1.58 (1.05, 2.38)		
2,4,5 T P	0 d	1071 (92.5)	Ref	0.06	
	<5 d	57 (4.9)	1.37 (1.01, 1.86)		
	5-9 d	15 (1.3)	0.98 (0.56, 1.72)		
	>10 d	15 (1.3)	1.70 (0.95, 3.03)		
Atrazine	0 d	473 (23.2)	Ref	0.95	
	<5 d	630 (30.9)	1.08 (0.95, 1.23)		
	5-9 d	546 (26.8)	1.13 (0.98, 1.30)		
	10-19 d	289 (14.2)	1.09 (0.92, 1.28)		
	20-39 d	87 (4.3)	1.11 (0.87, 1.43)		
	>40 d	14 (0.7)	0.76 (0.44, 1.33)		
Cyanazine	0 d	1008 (51.7)	Ref	0.53	
	<5 d	452 (23.2)	1.09 (0.96, 1.24)		
	5-9 d	303 (15.5)	1.05 (0.91, 1.21)		
	10-19 d	138 (7.1)	1.04 (0.85, 1.26)		
	>20 d	49 (2.5)	1.11 (0.82, 1.52)		
Metribuzin	0 d	605 (53.6)	Ref	0.10	
	<5 d	305 (27.0)	1.08 (0.92, 1.27)		
	5-9 d	160 (14.2)	1.07 (0.87, 1.31)		
	10-19 d	48 (4.3)	1.37 (0.99, 1.91)		
	>20 d	10 (0.9)	1.28 (0.65, 2.55)		

Abbreviation: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; CI, Confidence Intervals; EPTC, S-Ethyl dipropylthiocarbamate; OI, Olfactory Impairment; OR, Odds Ratio

Odds ratios are adjusted for age, sex, state of residence, education, smoking status, ever performed following tasks at least once each year (repair engines, replace asbestos brake linings, handle stored grain, work in swine confinement areas, weld and paint), and correlated pesticides (correlated ever-use of pesticides with Spearman correlation  $\geq 0.40$ )

<sup>a</sup>Exposure categories: Never-use (0d) and use categorized by average days per year of use

Supplementary table 7: Intensity-weighted lifetime days of use through the first follow-up in relation to self-reported olfactory impairment with onset reported  $\leq 10$  years before the third follow-up in the Agricultural Health Study (n=19,563)

Pesticide	Exposure <sup>a</sup>	OR (95% CI)	P-trend
Lindane	Never	Ref	0.001
	>0–328	1.24 (0.91, 1.70)	
	>328–1188	1.50 (1.12, 2.02)	
	>1188	1.56 (1.17, 2.09)	
Aldicarb	Never	Ref	0.70
	>0–630	1.09 (0.66, 1.80)	
	>630–2426	1.19 (0.71, 1.98)	
	>2426	0.88 (0.50, 1.54)	
Carbaryl	Never	Ref	0.55
	>0–395	1.18 (0.94, 1.48)	
	>395–2048	1.28 (1.01, 1.61)	
	>2048	1.18 (0.90, 1.55)	
Carbofuran	Never	Ref	0.87
	>0–347	1.27 (1.05, 1.54)	
	>347–1241	1.26 (1.04, 1.51)	
	>1241	1.01 (0.82, 1.24)	
Chlorpyrifos	Never	Ref	0.74
	>0–465	1.21 (1.03, 1.43)	
	>465–1776	1.13 (0.95, 1.34)	
	>1776	1.06 (0.89, 1.27)	
Coumaphos	Never	Ref	0.43
	>0–394	1.04 (0.75, 1.46)	
	>394–1382	1.27 (0.94, 1.73)	
	>1382	0.82 (0.56, 1.18)	
Diazinon	Never	Ref	0.11
	>0–324	1.43 (1.10, 1.86)	
	>324–1147	1.13 (0.85, 1.50)	
	>1147	1.29 (0.97, 1.71)	
Dichlorvos	Never	Ref	0.13
	>0–543	1.41 (1.09, 1.83)	
	>543–3923	1.11 (0.84, 1.48)	
	>3923	1.28 (0.96, 1.69)	
Fonofos	Never	Ref	0.09
	>0–438	1.01 (0.75, 1.37)	
	>438–1550	1.31 (1.00, 1.72)	
	>1550	1.26 (0.96, 1.66)	
Malathion	Never	Ref	0.52
	>0–384	1.18 (0.95, 1.47)	
	>384–1286	0.90 (0.71, 1.13)	
	>1286	0.95 (0.76, 1.19)	
Parathion	Never	Ref	0.01
	>0–327	1.46 (1.17, 1.83)	
	>327–1622	1.36 (1.09, 1.70)	
	>1622	1.54 (1.25, 1.91)	
Phorate	Never	Ref	0.20
	>0–315	1.05 (0.81, 1.34)	
	>315–1134	1.28 (1.01, 1.62)	

	>1134	0.82 (0.62, 1.07)	
Terbufos	Never	Ref	0.05
	>0–637	1.08 (0.90, 1.30)	
	>637–2300	0.98 (0.81, 1.18)	
	>2300	1.20 (1.01, 1.43)	
Permethrin (crops)	Never	Ref	0.00
	>0–267	1.06 (0.80, 1.41)	
	>267–1004	0.97 (0.72, 1.32)	
	>1004	1.47 (1.14, 1.89)	
Permethrin (animals)	Never	Ref	0.06
	>0–385	1.31 (1.02, 1.69)	
	>385–1478	1.39 (1.09, 1.78)	
	>1478	1.26 (0.98, 1.63)	
Aluminum Phosphide	Never	Ref	0.52
	>0–64	1.52 (0.86, 2.66)	
	>64–257	1.51 (0.85, 2.70)	
	>257	0.67 (0.29, 1.55)	
Ethylene Dibromide	Never	Ref	0.18
	>0–196	0.77 (0.36, 1.68)	
	>196–930	1.30 (0.70, 2.39)	
	>930	1.42 (0.80, 2.54)	
Methyl Bromide	Never	Ref	0.31
	>0–294	0.99 (0.72, 1.36)	
	>294–1260	1.07 (0.79, 1.46)	
	>1260	0.84 (0.60, 1.18)	
Benomyl	Never	Ref	0.06
	>0–350	1.69 (1.04, 2.75)	
	>350–1792	1.07 (0.59, 1.94)	
	>1792	1.76 (1.05, 2.97)	
Captan	Never	Ref	0.11
	>0–10	1.20 (0.90, 1.62)	
	>10–466	1.28 (0.96, 1.69)	
	>466	1.28 (0.97, 1.71)	
Chlorothalonil	Never	Ref	0.44
	>0–588	1.25 (0.83, 1.88)	
	>588–3276	1.22 (0.81, 1.83)	
	>3276	1.19 (0.78, 1.83)	
Maneb/Mancozeb	Never	Ref	0.59
	>0–432	0.89 (0.50, 1.56)	
	>432–2688	1.24 (0.75, 2.03)	
	>2688	1.14 (0.68, 1.91)	
Metalaxyll	Never	Ref	0.60
	>0–255	1.15 (0.84, 1.57)	
	>255–1323	1.02 (0.72, 1.46)	
	>1323	1.13 (0.77, 1.64)	
Alachlor	Never	Ref	0.18
	>0–784	0.99 (0.83, 1.17)	
	>784–2955	1.08 (0.91, 1.27)	
	>2955	1.11 (0.94, 1.31)	
Butylate	Never	Ref	0.32
	>0–455	1.08 (0.83, 1.41)	

	>455–1512	0.86 (0.64, 1.15)	
	>1512	1.17 (0.90, 1.53)	
Chlorimuron Ethyl	Never	Ref	0.62
	>0–248	1.07 (0.83, 1.38)	
	>248–735	1.03 (0.80, 1.33)	
	>735	1.07 (0.83, 1.37)	
Dicamba	Never	Ref	0.59
	>0–680	1.15 (0.96, 1.39)	
	>680–2352	1.24 (1.03, 1.50)	
	>2352	1.12 (0.93, 1.36)	
EPTC	Never	Ref	0.54
	>0–315	0.97 (0.76, 1.24)	
	>315–1176	1.14 (0.91, 1.43)	
	>1176	1.06 (0.83, 1.34)	
Glyphosate	Never	Ref	0.03
	>0–983	1.33 (1.06, 1.67)	
	>983–3402	1.35 (1.09, 1.68)	
	>3402	1.45 (1.16, 1.81)	
Imazethapyr	Never	Ref	0.66
	>0–400	0.98 (0.81, 1.19)	
	>400–1176	0.92 (0.76, 1.12)	
	>1176	0.96 (0.78, 1.17)	
Metolachlor	Never	Ref	0.25
	>0–765	1.23 (1.04, 1.45)	
	>765–2688	1.07 (0.90, 1.28)	
	>2688	0.95 (0.79, 1.14)	
Paraquat	Never	Ref	0.10
	>0–289	1.21 (0.88, 1.68)	
	>289–1171	1.21 (0.86, 1.69)	
	>1171	1.35 (0.95, 1.92)	
Pendimethalin	Never	Ref	0.40
	>0–354	0.98 (0.78, 1.22)	
	>354–1176	1.17 (0.95, 1.45)	
	>1176	1.08 (0.86, 1.35)	
Petroleum distillates	Never	Ref	0.05
	>0–490	1.17 (0.88, 1.56)	
	>490–2320	1.32 (1.00, 1.73)	
	>2320	1.31 (1.00, 1.73)	
Trifluralin	Never	Ref	0.24
	>0–1050	0.93 (0.77, 1.13)	
	>1050–3906	1.08 (0.89, 1.31)	
	>3906	1.09 (0.90, 1.33)	
2,4-D	Never	Ref	0.11
	>0–1511	1.20 (0.98, 1.46)	
	>1511–5428	1.12 (0.92, 1.37)	
	>5428	1.25 (1.02, 1.53)	
2,4,5-T	Never	Ref	0.19
	>0–289	1.76 (1.35, 2.31)	
	>289–971	1.56 (1.16, 2.09)	
	>971	1.30 (0.95, 1.76)	
Atrazine	Never	Ref	0.51

	>0–1232	1.06 (0.88, 1.28)		
	>1232–4550	1.05 (0.87, 1.26)		
	>4550	1.09 (0.90, 1.30)		
Cyanazine	Never	Ref	0.64	
	>0–540	1.18 (0.99, 1.42)		
	>540–2222	1.14 (0.95, 1.36)		
	>2222	1.09 (0.91, 1.31)		
Metribuzin	Never	Ref	0.50	
	>0–333	1.10 (0.86, 1.40)		
	>333–1040	1.01 (0.78, 1.31)		
	>1040	1.11 (0.86, 1.43)		

Abbreviation: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; CI, Confidence Intervals; EPTC, S-Ethyl dipropylthiocarbamate; OI, Olfactory Impairment; OR, Odds Ratio

Odds ratios are adjusted for age, sex, state of residence, education, smoking status, ever performed following tasks at least once each year (repair engines, replace asbestos brake linings, handle stored grain, work in swine confinement areas, weld and paint), and correlated pesticides (correlated ever-use of pesticides with Spearman correlation  $\geq 0.40$ )

\*Exposure categories: Never use and categorized into tertiles among users

**Supplementary table 8:** Ever-use of pesticide at enrollment in relation to self-reported olfactory impairment reported in the third follow-up in the Agricultural Health Study using inverse probability of censoring weights<sup>a</sup>

Pesticides	OR (95% CI)
<b>Insecticide</b>	
Organochlorine	
Aldrin	1.04 (0.88, 1.22)
Chlordane	1.09 (0.97, 1.23)
Dieldrin	1.22 (1.01, 1.49)
DDT	1.30 (1.14, 1.49)
Heptachlor	1.08 (0.91, 1.27)
Toxaphene	1.22 (1.07, 1.40)
Lindane	1.20 (1.07, 1.35)
Carbamate	
Aldicarb	1.01 (0.82, 1.25)
Carbaryl	1.25 (1.12, 1.41)
Carbofuran	1.13 (1.01, 1.26)
Organophosphate	
Chlorpyrifos	1.13 (1.02, 1.25)
Coumaphos	1.07 (0.92, 1.26)
Diazinon	1.09 (0.97, 1.22)
Dichlorvos	1.22 (1.06, 1.40)
Fonofos	0.98 (0.87, 1.10)
Malathion	1.32 (1.17, 1.50)
Parathion	1.22 (1.07, 1.40)
Phorate	1.00 (0.89, 1.11)
Terbufos	1.07 (0.96, 1.19)
Permethrin (crops)	1.28 (1.10, 1.47)
Permethrin (animals)	1.2 (1.05, 1.38)
Fumigant	
CCl <sub>4</sub> /CS <sub>2</sub>	1.37 (1.13, 1.65)
Aluminum phosphide	1.07 (0.87, 1.32)
Ethylene dibromide	0.81 (0.62, 1.07)
Methyl bromide	0.97 (0.80, 1.18)
Fungicide	
Benomyl	0.90 (0.71, 1.16)
Captan	1.25 (1.08, 1.44)
Chlorothalonil	1.39 (1.09, 1.77)
Maneb	1.16 (0.93, 1.45)
Metalaxyl	1.14 (0.99, 1.32)
Herbicide	
Alachlor	1.04 (0.93, 1.15)
Butylate	1.05 (0.93, 1.18)
Chlorimuron ethyl	0.99 (0.89, 1.10)
Dicamba	1.11 (0.99, 1.25)
EPTC	1.07 (0.94, 1.20)
Glyphosate	1.34 (1.18, 1.53)
Imazethapyr	0.93 (0.82, 1.04)
Metolachlor	1.01 (0.91, 1.11)
Paraquat	1.12 (0.98, 1.28)
Pendimethalin	1.03 (0.93, 1.14)
Petroleum distillates	1.14 (1.03, 1.27)

Trifluralin	1.09 (0.96, 1.23)
2,4-D	1.11 (0.97, 1.28)
2,4,5-T	1.25 (1.09, 1.43)
2,4,5-TP	0.85 (0.71, 1.03)
Atrazine	1.09 (0.96, 1.24)
Cyanazine	1.02 (0.91, 1.13)
Metribuzin	1.03 (0.91, 1.16)

Abbreviation: 2,4-D, 2,4-Dichlorophenoxyacetic acid; 2,4,5-T, 2,4,5-Trichlorophenoxyacetic acid; 2,4,5-T,P, 2-(2,4,5-trichlorophenoxy) propionic acid; CI, Confidence Intervals; CCl<sub>4</sub>/CS<sub>2</sub>, Carbon tetrachloride/Carbon disulfide 80/20 mix; DDT, Dichlorodiphenyltrichloroethane; EPTC, S-Ethyl dipropylthiocarbamate; OI, Olfactory Impairment; OR, Odds Ratio

Odds ratios are adjusted for age, sex, state of residence, education, smoking status, ever performed following tasks at least once each year (repair engines, replace asbestos brake linings, handle stored grain, work in swine confinement areas, weld and paint), and correlated pesticides (correlated ever-use of pesticides with Spearman correlation  $\geq 0.40$ )

<sup>a</sup>Numerator of stabilized weights estimated as a marginal probability of overall participation in the third follow-up and denominator estimated as a probability of overall participation conditional on specific pesticide (that considered as exposure), age, sex, state of residence, education, smoking status, and ever performed following tasks at least once each year (repair engines, replace asbestos brake linings, handle stored grain, work in swine confinement areas, weld and paint)